NATIONAL DEFENSE RESEARCH INSTITUTE

Mindfulness-Based Relapse Prevention for Substance Use Disorders

A Systematic Review

Sean Grant, Susanne Hempel, Benjamin Colaiaco, Aneesa Motala, Roberta M. Shanman, Marika Booth, Whitney Dudley, Melony E. Sorbero

Prepared for the Office of the Secretary of Defense

Report Documentation Page

Form Approved
OMB No. 0704-0188

1. REPORT DATE	2. REPORT TYPE	3. DATES COVERED
2015		**00-00-2015 to 00-00-2015**

4. TITLE AND SUBTITLE	5a. CONTRACT NUMBER
Mindfulness-Based Relapse Prevention for Substance Use Disorders: A Systematic Review	5b. GRANT NUMBER
	5c. PROGRAM ELEMENT NUMBER
6. AUTHOR(S)	5d. PROJECT NUMBER
	5e. TASK NUMBER
	5f. WORK UNIT NUMBER
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) **RAND Corporation,National Defense Research Institute,1776 Main Street, P.O. Box 2138,Santa Monica,CA,90407-2138**	8. PERFORMING ORGANIZATION REPORT NUMBER
9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)	10. SPONSOR/MONITOR'S ACRONYM(S)
	11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION/AVAILABILITY STATEMENT
Approved for public release; distribution unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

This systematic review aims to synthesize evidence from trials of Mindfulness-Based Relapse Prevention (MBRP) to provide estimates of its efficacy and safety for substance use disorders (PROSPERO record CRD42015016380). In December 2014, we searched PubMed, PsycINFO, AMED, CINAHL, CENTRAL, Web of Science, and bibliographies of existing systematic reviews and included studies to identify English-language randomized controlled trials (RCTs) evaluating the efficacy and safety of MBRP???used adjunctively or as monotherapy???to treat substance use disorders in adults diagnosed with alcohol, opioid, stimulant, and/or cannabis use disorder. Two independent reviewers screened identified literature using predetermined eligibility criteria, abstracted prespecified study-level information and outcome data, and assessed the quality of included studies. Outcomes of interest included relapse, frequency and quantity of substance use withdrawal/craving symptoms, treatment dropout, functional status, health-related quality of life recovery outcomes, and adverse events. When possible, meta-analyses were conducted using the Hartung-Knapp-Sidik-Jonkman method for random-effects models. Strength of evidence was assessed using the GRADE approach. Six studies (reported in 20 publications) with 685 participants were included. Evidence was insufficient to determine whether MBRP effects differ by type of substance use targeted. There were no significant effects for MBRP as an adjunctive therapy or a standalone monotherapy for most outcomes; we did find some evidence in support of MBRP evaluated as an adjunctive therapy based on one RCT with regard to quality of life (SMD ???0.65; CI ???1.20 to ???0.10; 1 RCT very low quality evidence) and legal problems (SMD ???1.20; CI ???1.78 to ???0.62; 1 RCT, very low quality evidence), yet these outcomes were not measured in any RCTs of MBRP as a monotherapy to serve as a comparison with effects for MBRP as an adjunctive therapy. Effects did not appear to systematically differ by identified comparison group. Across studies, we did not find differences between MBRP and any comparator (standard relapse prevention, cognitive behavioral therapy, or treatment as usual) for relapse (OR 0.49; CI 0.17 to 1.44; 4 RCTs) or other outcomes except for quality of life (as above). Three RCTs reported on adverse events: Two RCTs reported no adverse events, while the third reported that one participant receiving standard relapse prevention died, and another participant receiving MBRP was admitted to inpatient care. There were no statistically significant differences between MBRP and any of the comparators for substance use outcomes. The available evidence on MBRP effects is very limited, both in terms of the quantity of existing studies and the quality of the body of evidence. To provide firmer conclusions about the efficacy and safety of MBRP, future

15. SUBJECT TERMS

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			
unclassified	**unclassified**	**unclassified**	**Same as Report (SAR)**	**78**	

For more information on this publication, visit www.rand.org/t/RR1031

Published by the RAND Corporation, Santa Monica, Calif.

Preface

The Defense Centers of Excellence for Psychological Health and Traumatic Brain Injury is interested in determining the efficacy and comparative effectiveness of integrative medicine approaches for psychological health conditions. This document is a systematic review of Mindfulness-Based Relapse Prevention for substance use disorders, conducted in year two of this two-year project. The review will be of interest to military health policymakers and practitioners, civilian health care providers and policymakers, payers, and patients.

A version of this report was provided to the committee for review in March 2015; we reproduce that version here, with minor editorial updates. None of the authors has any conflict of interest to declare.

This research was sponsored by the Defense Centers of Excellence for Psychological Health and Traumatic Brain Injury and conducted within the Forces and Resources Policy Center of the RAND National Defense Research Institute, a federally funded research and development center sponsored by the Office of the Secretary of Defense, the Joint Staff, the Unified Combatant Commands, the Navy, the Marine Corps, the defense agencies, and the defense Intelligence Community. For more information on the RAND Forces and Resources Policy Center, see http://www.rand.org/nsrd/ndri/centers/frp.html or contact the director (contact information is provided on the web page).

Abstract

This systematic review aims to synthesize evidence from trials of Mindfulness-Based Relapse Prevention (MBRP) to provide estimates of its efficacy and safety for substance use disorders (PROSPERO record CRD42015016380).

In December 2014, we searched PubMed, PsycINFO, AMED, CINAHL, CENTRAL, Web of Science, and bibliographies of existing systematic reviews and included studies to identify English-language randomized controlled trials (RCTs) evaluating the efficacy and safety of MBRP—used adjunctively or as monotherapy—to treat substance use disorders in adults diagnosed with alcohol, opioid, stimulant, and/or cannabis use disorder. Two independent reviewers screened identified literature using predetermined eligibility criteria, abstracted pre-specified study-level information and outcome data, and assessed the quality of included studies. Outcomes of interest included relapse, frequency and quantity of substance use, withdrawal/craving symptoms, treatment dropout, functional status, health-related quality of life, recovery outcomes, and adverse events. When possible, meta-analyses were conducted using the Hartung-Knapp-Sidik-Jonkman method for random-effects models. Strength of evidence was assessed using the GRADE approach.

Six studies (reported in 20 publications) with 685 participants were included. Evidence was insufficient to determine whether MBRP effects differ by type of substance use targeted. There were no significant effects for MBRP as an adjunctive therapy or a standalone monotherapy for most outcomes; we did find some evidence in support of MBRP evaluated as an adjunctive therapy based on one RCT with regard to quality of life (SMD −0.65; CI −1.20 to −0.10; 1 RCT; very low quality evidence) and legal problems (SMD −1.20; CI −1.78 to −0.62; 1 RCT, very low quality evidence), yet these outcomes were not measured in any RCTs of MBRP as a monotherapy to serve as a comparison with effects for MBRP as an adjunctive therapy. Effects did not appear to systematically differ by identified comparison group. Across studies, we did not find differences between MBRP and any comparator (standard relapse prevention, cognitive behavioral therapy, or treatment as usual) for relapse (OR 0.49; CI 0.17 to 1.44; 4 RCTs) or other outcomes except for quality of life (as above). Three RCTs reported on adverse events: Two RCTs reported no adverse events, while the third reported that one participant receiving standard relapse prevention died, and another participant receiving MBRP was admitted to inpatient care.

There were no statistically significant differences between MBRP and any of the comparators for substance use outcomes. The available evidence on MBRP effects is very limited, both in terms of the quantity of existing studies and the quality of the body of evidence. To provide firmer conclusions about the efficacy and safety of MBRP, future RCTs on this intervention are needed.

Table of Contents

Figures

Tables

Summary

Introduction

Relapsing to substance use following treatment is highly prevalent among U.S. adults, necessitating interventions that target reversion to substance use. Mindfulness-Based Relapse Prevention (MBRP) was developed to increase the effectiveness of relapse prevention therapy by incorporating mindfulness-based meditation practices. The systematic review in this report aims to synthesize evidence from trials of MBRP to provide estimates of its effectiveness for substance use relapse. The PROSPERO number for protocol is CRD42015016380. PROSPERO is an international database of prospectively registered systematic reviews in health and social care.

This review was specifically guided by the following key questions (KQs):

- *KQ 1*: What is the efficacy and safety of MBRP, as an adjunctive or monotherapy, for adults with alcohol, opioid, stimulant, or cannabis use disorders compared with treatment as usual (TAU), wait lists, no treatment, or other active treatments?
  - *KQ 1a*: Does the effect of MBRP vary by the substance targeted (i.e., alcohol, opioids, stimulants, or cannabis)?
  - *KQ 1b*: Does the effect of MBRP differ if MBRP is offered as an adjunctive therapy rather than as a monotherapy?
  - *KQ 1c*: Does the effect of MBRP on substance use disorders (SUDs) depend on the comparator?

For these key questions, the specific efficacy outcomes of interest included relapse, frequency and quantity of substance use, withdrawal or craving symptoms, treatment dropout, functional status, and health-related quality of life. Safety was evaluated with regard to reported adverse events.

Methods

To answer our key questions, we conducted a systematic search in December 2014 of electronic databases (PubMed, PsycINFO, CINAHL, AMED, CENTRAL, and Web of Science,), as well as bibliographies of existing systematic reviews and included studies, to identify English-language reports of randomized controlled trials (RCTs) testing the efficacy and safety of MBRP—used adjunctively or as a monotherapy—to treat individuals with SUDs. Participants must have been 18 years or older and diagnosed with alcohol, opioid, stimulant, and/or cannabis use disorder. There were no exclusion criteria regarding comparison intervention or trial setting.

Two independent reviewers screened the identified literature using predetermined eligibility criteria, abstracted pre-specified study-level information and outcome data, and assessed the quality of included studies. Outcomes of interest included relapse, frequency and quantity of

substance use, withdrawal/craving symptoms, treatment dropout, functional status, health-related quality of life, recovery outcomes, and adverse events. When possible, meta-analyses were conducted using the Hartung-Knapp-Sidik-Jonkman method for random-effects models. Quality of evidence was assessed using the Grades of Recommendation, Assessment, Development, and Evaluation, or GRADE, approach.

Results

We identified six eligible RCTs (reported in 20 publications) with 685 total participants. The length of outcome follow-up ranged from immediately postintervention to 12-month follow-up postintervention. The length of MBRP ranged from eight to 16 hours of intervention sessions total. All RCTs took place in SUD specialty care settings. Five RCTs took place in the United States, and one took place in Taiwan. Participants' average age ranged from approximately 35.8 to 40.7 years old. One RCT contained only females, and another contained only males; of the remaining four RCTs, the proportion of males ranged from 63.7 percent to 72.7 percent.

Key Question 1

We identified five RCTs providing data on the overall efficacy of MBRP for adults with SUDs, though studies did not consistently measure outcome domains of interest to this review. Across all studies, we did not find evidence in support of MBRP for relapse (odds ratio [OR] 0.49; 95-percent confidence interval [CI] 0.17 to 1.44; 4 RCTs), frequency of substance use (standardized mean difference [SMD] −0.09; CI −0.66 to 0.49; 4 RCTs), withdrawal/craving symptoms (SMD −0.14; CI −0.50 to 0.22; 1 RCT), functional status (SMD −0.24; CI −2.04 to 1.56; 2 RCTs), and number of participants incarcerated (OR 0.53; CI 0.06 to 5.01; 2 RCTs) comparing MBRP (as an adjunctive or monotherapy) versus any comparator. (Note: All CIs reported in this study are at the 95-percent level.) We did identify a significant effect in favor of MBRP for health-related quality of life (SMD −0.65; CI −1.20 to −0.10; 1 RCT) compared with standard relapse prevention—though this result is based on very low quality of evidence. No studies provided outcome data on quantity of substance use. Three RCTs reported on adverse events: Two reported no adverse events, while the third reported that one participant receiving standard relapse prevention died, and another participant receiving MBRP was admitted to inpatient care for reasons unknown.

Key Question 1a

For KQ 1a on the effect of MBRP by substance targeted, all trials involved polysubstance using participant samples; of these, we identified two RCTs providing information on alcohol use specifically and one RCT on stimulant use; no RCTs provided information about opioid or cannabis use specifically. We did not find any direct comparisons of MBRP for one substance versus another. There was very low-quality evidence of a statistically significant effect on

relapse to alcohol use for MBRP (as a monotherapy) versus TAU at six-month follow-up (OR 0.35; CI 0.14 to 0.88; 1 RCT). We found no statistically significant effects of MBRP on frequency of alcohol use (SMD 0.30; CI −6.45 to 7.05; 2 RCTs) and frequency of stimulant use (SMD 0.77; CI −0.36 to 1.90; 1 RCT). We thus identified no strong or consistent evidence suggesting that MBRP effects differ by type of substance targeted.

Key Question 1b

For KQ 1b on the effect of MBRP as an adjunctive therapy versus a monotherapy, we identified two RCTs providing data on MBRP as an adjunctive therapy, and three providing data on MBRP as a monotherapy. There was low-quality evidence suggesting that MBRP offered as a monotherapy versus an adjunctive therapy yields different effects for some outcomes. We found no direct evidence comparing MBRP as a monotherapy versus MBRP as an adjunctive therapy; we consequently conducted an indirect comparison of the results of analyses of MBRP as a monotherapy (versus comparator interventions) to MBRP as an adjunctive therapy (versus comparator interventions). We did not find effects of MBRP as a monotherapy (versus any comparator) on relapse (OR 0.56; CI 0.00 to 992.23; 2 RCTs), frequency of substance use (SMD 0.00; CI −1.03 to 1.03; 3 RCTs), withdrawal/craving symptoms (SMD −0.14; CI −0.50 to 0.22; 1 RCT), treatment dropout (OR 0.76; CI 0.27 to 2.18; 2 RCTs), functional status (SMD −0.14; CI −0.50 to 0.21; 1 RCT), or recovery outcomes (OR 0.53; CI 0.06 to 5.01; 2 RCTs). In contrast, for MBRP as an adjunctive therapy, we found statistically significant effects (versus standard relapse prevention) for health-related quality of life (SMD −0.65; CI −1.20 to −0.10) and legal problems (SMD −1.20; CI −1.78 to −0.62), but results were based on one RCT only. The quality of this evidence was also determined to be very low (health-related quality of life and legal problems) due to high attrition bias, inability to judge consistency across multiple RCTs, and/or wide confidence intervals spanning effect sizes with different clinical conclusions. Moreover, there was no evidence of a statistically significant effect of MBRP (as an adjunctive therapy) for substance use relapse (OR 0.42; CI 0.00 to 62.17; 2 RCTs), frequency of substance use (SMD −0.36; CI −0.90 to 0.18; 1 RCT), treatment dropout (OR 1.47; CI 0.64 to 3.36; 1 RCT), and functional status (SMD −0.45; CI −0.99 to 0.09; 1 RCT).

Key Question 1c

For KQ 1c on whether the effect of MBRP is dependent on the type of comparator, we identified one RCT comparing the effects of MBRP with standard relapse prevention and with TAU. Three RCTs provided data on MBRP versus an active comparator (two were standard relapse prevention, one was cognitive behavioral therapy), and three RCTs provided data on MBRP versus TAU (two were modeled after 12-step facilitation, one was the Matrix Model). MBRP effects did not appear to systematically differ by comparison group: There was no evidence of effects of MBRP when compared with any TAU or active comparator, except for the outcome quality of life. The effect in favor of MBRP was based on the comparison with a

standard relapse prevention intervention (SMD −0.65; CI −1.20 to −0.10; RCT), and we found no evidence on MBRP versus TAU for this outcome.

Conclusions

Overall, the available evidence in support of MBRP is very limited. There were no consistent differences between MBRP and any of the comparators for substance use outcomes; moreover, the number of available studies is small, and the quality of this evidence is very low. The available evidence on adverse events is also very limited; two RCTs reported that no adverse events occurred, while a third reported that one participant receiving standard relapse prevention died, and another participant receiving MBRP was admitted to inpatient care for reasons unknown. However, it is possible that adverse events occurred in the three studies that did not address adverse events in their reports. The review indicates positive results for MBRP as an adjunctive therapy for health-related quality of life and legal problems; however, given that these results were based on one RCT without replication, there is uncertainty in the magnitude and stability of effect estimates. To provide firmer conclusions about the efficacy and safety of MBRP, future RCTs on this intervention are needed.

Acknowledgments

This research is sponsored by the Defense Centers of Excellence for Psychological Health and Traumatic Brain Injury (DCoE). We gratefully acknowledge Kristie Gore for her support and guidance throughout the project. We also would like to thank our project officers and points of contact at DCoE—Chris Crowe, Marina Khusid, and Michael Freed—for their support of our work, as well as the quality assurance reviewers—Paul Shekelle and Tracy Simpson—for their time and helpful suggestions. Any errors of fact or interpretation in this report remain the responsibility of the authors.

Abbreviations

AMED	Allied and Complementary Medicine Database
CBT	cognitive behavioral therapy
CENTRAL	Cochrane Central Register of Controlled Trials
CI	confidence interval
CINAHL	Cumulative Index to Nursing and Allied Health Literature
DSM	*Diagnostic and Statistical Manual of Mental Disorders*
GRADE	Grades of Recommendation, Assessment, Development, and Evaluation
HR	hazard ratio
ICD	International Classification of Diseases
KQ	key question
MBRP	Mindfulness Based Relapse Prevention
MORE	mindfulness-oriented recovery enhancement
OR	odds ratio
RCT	randomized controlled trial
RP	relapse prevention
RR	risk ratio
SD	standard deviation
SMD	standardized mean difference
SUD	substance use disorder
TAU	treatment as usual
TLFB	Time Line Follow Back

Chapter One: Introduction

Description of the Condition

Relapsing to substance use following treatment is highly prevalent among U.S. adults. Depending on the type of substance and severity of use considered, 7 to 20 percent of U.S. adults have a substance use disorder (SUD) in a given year (Grant et al., 2004; Compton et al., 2007; Hasin et al., 2007; Kessler et al., 2005; Substance Abuse and Mental Health Services Administration, 2011). However, only 10 percent of U.S. adults with SUDs actually seek treatment (Substance Abuse and Mental Health Services Administration, 2008), and 40 to 60 percent of those receiving treatment experience relapse within 12 months (McLellan et al., 2000). Consequently, interventions are needed that specifically address the chronic relapsing nature of SUDs (Connors, Maisto, and Donovan, 1996).

Relapse prevention therapy (Marlatt and Gordon, 1985) is a widely implemented approach (Brandon, Vidrine, and Litvin, 2007) with demonstrated effectiveness in reducing risk of relapse to substance use (Carroll, 1996; Irvin et al., 1999; Lancaster et al., 2006). The theory of change underlying relapse prevention is that interactions between the individual and the environment can increase the risk of relapse, such as social influences, greater access to substances, and an individual's inability to cope with craving (Witkiewitz and Marlatt, 2004). With this framework in mind, practitioners delivering relapse prevention therapy help the client to identify situations that trigger relapse and teach clients cognitive and behavioral skills to reduce the risk of relapse (Marlatt and Gordon, 1985).

Description of the Intervention

Mindfulness-Based Relapse Prevention (MBRP) is a specific treatment approach developed by researchers at the Addictive Behaviors Research Center, University of Washington, for individuals in recovery from SUD behaviors (Bowen, Chawla, and Marlatt, 2010). It incorporates mindfulness-based meditation with relapse prevention techniques, with the goal of decreasing the risk and severity of relapse to substance use following treatment. MBRP involves identifying individual risk factors or common precursors to relapse; recognizing underlying reasons for maladaptive substance use; teaching meditation practices to increase awareness of and change one's relation to challenging emotional, cognitive, and physical states arising from craving or withdrawal from substance use; and providing skills to tolerate these states (Bowen, Chawla, and Marlatt, 2010; Bowen, Chawla, and Witkiewitz, 2014).

How the Intervention Might Work

Through assisting the client with internal experiences related to substance use relapse, MBRP is hypothesized to increase acceptance and tolerance of internal distress associated with substance use cues, decrease subjective feelings of urgency to alleviate this distress by using substances, and thereby decouple such negative affects and substance use (Witkiewitz and Bowen, 2010).

Why It Is Important to Do This Review

The current Department of Veterans Affairs and Department of Defense Clinical Practice Guideline on the Management of Substance Use Disorders does not cover the use of MBRP (Management of Substance Use Disorders Working Group, 2009). Several randomized controlled trials (RCTs) evaluating the effectiveness of MBRP in reducing relapse risk have been conducted (Bowen, Chawla, et al., 2009; Bowen, Witkiewitz, Clifasefi, et al., 2014; Lee, Bowen, and Bai, 2011; Witkiewitz and Bowen, 2010), and overviews of mindfulness-based meditation approaches more generally suggest efficacy and safety for SUDs (Zgierska et al., 2009). However, no study has systematically reviewed all RCTs of MBRP.

Objective

This review aims to synthesize evidence from RCTs of MBRP in order to provide reliable estimates of the effectiveness and safety of MBRP for SUDs.

Chapter Two: Methods

Key Questions

We conducted a systematic review to identify RCTs testing the efficacy and safety of MBRP in treating individuals with SUDs. (The PROSPERO number for protocol is CRD42015016380. PROSPERO is an international database of prospectively registered systematic reviews in health and social care.) Specifically, this systematic review aimed to answer the following key questions (KQs):

- *KQ 1*: What is the efficacy and safety of MBRP, as an adjunctive or monotherapy, for adults with alcohol, opioid, stimulant, or cannabis use disorders compared with treatment as usual (TAU), wait lists, no treatment, or other active treatments?
  - *KQ 1a*: Does the effect of MBRP vary by the substance targeted (i.e., alcohol, opioids, stimulants, or cannabis)?
  - *KQ 1b*: Does the effect of MBRP differ if MBRP is offered as an adjunctive therapy rather than as a monotherapy?
  - *KQ 1c*: Does the effect of MBRP on SUDs depend on the comparator?

For these key questions, the specific efficacy outcomes of interest included relapse, frequency and quantity of substance use, withdrawal/or craving symptoms, treatment dropout, functional status, recovery outcomes, and health-related quality of life. Safety was evaluated with regard to reported adverse events.

Search Strategy

The research team searched the following databases for studies published from 2000 through December 9, 2014: PubMed, PsycINFO, CINAHL, AMED, CENTRAL, and Web of Science. The search combined terms on mindfulness-based meditation, alcohol and other drugs, and abuse or dependence criteria (see Appendix A). We decided to search databases from 2000 onward because MBRP was developed in the past 15 years (Bowen, Chawla, and Marlatt, 2010) and the evaluations of mindfulness-based approaches for SUDs are therefore recent (Zgierska et al., 2009). The chief reference librarian for RAND's Knowledge Services developed the search strings for each database, informed by search results of an environmental scan of the literature at the initiation of this study (as part of unpublished RAND research by Melony Sorbero, Sean Grant, and Susanne Hempel), as well as by the search strings of previous reviews (Chiesa and Serretti, 2014; Goyal et al., 2014; Skanavi, Laqueille, and Aubin, 2011; Zgierska et al., 2009). Reference lists from previous reviews of mindfulness meditation for SUDs, as well as from included studies, were also examined. We included search terms on substance misuse, abuse, and

dependence in order for the search strategy to reflect the review's eligibility criteria—that participants must have been diagnosed with a substance abuse or dependence disorder (see next section). Our systematic search strategy identified MBRP RCTs that were not found by existing reviews and included studies, as well as one ongoing RCT of MBRP; therefore, we believe that our search strategy reflects a comprehensive search of this literature.

Eligibility Criteria

Inclusion and exclusion criteria for this review were developed using the framework of participants, interventions, comparators, outcomes, timing, settings, and study design, or PICOTSS:

- *Participants*: Studies were limited to adults, male and female, who are 18 years of age or older. Participants must have been diagnosed with alcohol, opioid, stimulant, and/or cannabis use disorder. Diagnoses include abuse or dependence using the *Diagnostic and Statistical Manual of Mental Disorders* (DSM)-IV criteria, SUD using DSM-V criteria, or harmful use or dependence syndrome using International Classification of Diseases (ICD) criteria.
- *Interventions*: Studies that administered MBRP, either as a monotherapy or as an adjunctive therapy (interventions combining mindfulness-based meditation with relapse prevention strategies), were included. Studies must have either identified the intervention as MBRP or described the components of the intervention as explicitly combining mindfulness-based meditation with standard relapse prevention (Marlatt and Gordon, 1985). Studies involving other mindfulness-based interventions, such as mindfulness-based cognitive therapy or mindfulness-based stress reduction, were excluded, unless standard relapse prevention (Marlatt and Gordon, 1985) was also provided.
- *Comparators*: Studies were not limited by comparator. Studies that included TAU or "standard care," wait list control, no treatment, or other active treatments, or that compared MBRP administered as an adjunctive therapy versus a monotherapy, were included.
- *Outcomes*: Studies that reported on patient outcomes such as relapse, frequency of substance use, quantity of substance use, withdrawal or craving symptoms, treatment dropout, change in functional status, change in recovery outcomes, change in health-related quality of life, and adverse events were included.
- *Timing*: Studies could have involved any treatment duration and follow-up period.
- *Setting*: Studies were not limited by setting (e.g., country, physical location of treatment).
- *Study design***:** Included studies were limited to parallel group controlled trials that were individually or cluster-randomized.

Inclusion Screening

Two independent reviewers from RAND (the project lead, who is a doctoral-level experienced systematic reviewer, and a RAND research assistant with experience in systematic reviews) screened titles and abstracts of retrieved citations. An initial session piloting the screening form occurred prior to these reviews to ensure similar interpretation of the inclusion

and exclusion criteria. Citations judged as potentially eligible by one or both reviewers were obtained as full text. The full-text publications were then screened against the specified inclusion criteria by the two independent reviewers; any disagreements were resolved through discussion within the review author team.

Data Extraction

The two aforementioned reviewers each independently abstracted study-level data in an electronic database. The project lead designed data collection forms with input from the project team. The two reviewers pilot-tested the data collection forms on a few well-reported studies to ensure agreement of interpretation. The project lead abstracted all outcome data, which was checked by a biostatistician at the RAND Evidence-based Practice Center for accuracy.

The following information was abstracted from each study:

- *Participants*: gender, age, baseline substance use, and comorbid psychological/behavioral health conditions
- *Interventions*: content of MBRP sessions, dosage (intensity, frequency, duration), format (individual, group), and co-intervention(s)
- *Comparators*: type of comparator
- *Outcomes assessed*: relapse, frequency and quantity of substance use, withdrawal or craving symptoms, treatment dropout, functional status, health-related quality of life, and adverse events for each time point of measurement; for each outcome, we abstracted data on domain (e.g., frequency of substance use), method of measurement (e.g., Time Line Follow Back [TLFB]), metric of data expression (e.g., means, proportions), primary endpoint (e.g., six-month follow-up), and corresponding results (i.e., effect estimate, precision)
- *Timing*: time-points of outcome assessment and timing of intervention administration (e.g., aftercare)
- *Setting*: geographic region, type of health care setting (general health care setting versus specialty SUD care), and number of sites
- *Study design*: aim of study, inclusion and exclusion criteria, sample size, reported power calculations, and items relevant to risk of bias and quality ratings.

When several reports for the same study existed, we compared descriptions of participants to ensure that data from the same study populations entered analysis and synthesis only once. This situation occurred for three studies (see Table 3.2).

Risk of Bias

The two reviewers assessed the risk of bias of included studies using the Cochrane Risk of Bias tool (Higgins et al., 2011). Specifically, the reviewers assessed risks of bias related to the following domains: random sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and providers (performance bias), blinding of outcome

assessors (detection bias), completeness of reporting outcome data (attrition bias), and selective outcome reporting (reporting bias). Involvement of the developers of the program (Bowen, Chawla, and Marlatt, 2010) in the RCT was also assessed to indicate whether the RCT was an independent replication of previous efficacy trials.

Other biases related to the U.S. Preventive Services Task Force's (2008) criteria for internal validity of included studies were also assessed, namely those related to equal distribution among groups of potential confounders at baseline; crossovers or contamination between groups; equal, reliable, and valid outcome measurement; clear definitions of interventions; and intention-to-treat analysis. These criteria were used to rate the quality of evidence of individual included studies using the following guidelines (Lewin Group and ECRI Institute, 2014; U.S. Preventive Services Task Force, 2008):

- *Good*: Comparable groups are initially assembled and maintained throughout the study with at least 80-percent follow-up; reliable, valid measurement is used and applied equally to all groups; interventions are clearly described; all important outcomes are considered; appropriate attention is given to confounders in analysis; intention-to-treat analysis is used.
- *Fair*: One or more of the following issues is found in the study: some though not major differences between groups exist at follow-up; measurement instruments are acceptable but not ideal, though are generally applied equally; some but not all important outcomes are considered; some but not all potential confounders are accounted for in analyses. In addition, intention-to-treat analysis must be done.
- *Poor*: One or more of the following "fatal flaws" is found in the study: initially assembled groups are not comparable or maintained throughout the study; unreliable or invalid measurements are used or applied unequally across groups; key confounders are given little to no attention in analyses; intention-to-treat analysis is not used.

Data Synthesis

The primary aim of this systematic review is to identify whether MBRP is effective and safe in reducing relapse, frequency and quantity of substance use, withdrawal or craving symptoms, treatment dropout, and adverse events, as well as in improving functional status, recovery outcomes, and health-related quality of life, in adults with SUDs, compared with usual care. Therefore, when sufficient data were available, we performed random-effects meta-analyses to pool effectiveness results across included studies for the outcomes of interest. We used the Hartung-Knapp-Sidik-Jonkman method for our random-effects meta-analysis (Hartung, 1999; Hartung and Knapp, 2001; Sidik and Jonkman, 2006). This method may be preferred when the number of studies pooled is small and when there is evidence of heterogeneity (IntHout, Ioannidis, and Borm, 2014). It has been shown that the error rates are more robust than the previously used DerSimonian and Laird method (Sánchez-Meca and Marín-Martínez, 2008). Outcomes were grouped by length of follow-up (0–11 months, 12+ months).

In addition, we examined whether there are differences in effect sizes between studies conducted in different population groups—namely, by alcohol, opioid, stimulant, or cannabis use; by MBRP as a monotherapy versus as an adjunctive therapy; and by type of comparison group in the RCT. These analyses are particularly suited for when statistical heterogeneity (as measured using I^2) is below agreed thresholds (Higgins and Green, 2011). Given the complexity of the topic, subgroup and sensitivity analyses were performed only for those outcomes with sufficient data. For meta-analysis of data with clear outliers, sensitivity analyses were conducted (i.e., excluding the outliers) if appropriate.

Quality of Evidence

The quality of evidence was assessed for major outcomes using the Grades of Recommendation, Assessment, Development, and Evaluation (or GRADE) approach (Berkman et al., 2014; Lewin Group and ECRI Institute, 2014). Namely, the body of evidence was assessed based on the following dimensions: study limitations (low, medium, or high), directness (direct or indirect), consistency (consistent, inconsistent, or unknown), and precision (precise or imprecise) (Egger et al., 1997). For this review, we assessed study limitations, via the risk-of-bias assessments detailed above; directness, via how well various aspects of studies (e.g., population, intervention, comparator) address this review's key questions; consistency, via the magnitude of heterogeneity; and precision, via the width of confidence intervals. Using these criteria, the quality of evidence was graded on the following four-item scale:

- *High* indicates that the review authors are very confident that the effect estimate lies close to the true effect for a given outcome, as the body of evidence has few or no deficiencies. As such, the reviewers believe the findings are stable. That is, further research is very unlikely to change confidence in the effect estimate.
- *Moderate* indicates that the review authors are moderately confident that the effect estimate lies close to the true effect for a given outcome, as the body of evidence has some deficiencies. As such, the reviewers believe that the findings are likely to be stable, but further research may change confidence in the effect estimate and may even change the estimate.
- *Low* indicates that the review authors have limited confidence that the effect estimate lies close to the true effect for a given outcome, as the body of evidence has major or numerous (or both) deficiencies. As such, the reviewers believe that additional evidence is needed before concluding either that the findings are stable or that the effect estimate lies close to the true effect.
- *Very low* indicates that the review authors have very little confidence that the effect estimate lies close to the true effect for a given outcome, as the body of evidence has very major deficiencies. As such, the true effect is likely to be substantially different from the estimated effect; thus, any estimate of effect is very uncertain.

Chapter Three: Results

Results of the Search

We identified 58 records through our electronic search of databases and five records through reference mining of included studies and nine previous systematic reviews related to mindfulness meditation. After deduplication, we examined 59 titles and abstracts (see Figure 3.1).

Full texts were obtained for 27 records identified as potentially eligible by the two reviewers. Of these, seven articles were excluded at the full-text review, because they either did not include MBRP (n = 3) or did not involve a parallel group controlled trial that was individually randomized or cluster-randomized (n = 4). One study on Mindfulness-Oriented Recovery Enhancement (MORE) required review team discussion regarding eligibility, given that it did have mindfulness and relapse prevention components (Garland et al., 2010); it was ultimately decided to exclude this article, because the developers of MORE distinguish the program from other mindfulness-based treatments and do not primarily focus on relapse prevention (Garland, 2013). Another excluded study was a nonrandomized pilot of a new intervention that included MBRP; the results of this pilot will inform a future RCT (Florida, 2014). A list of the seven excluded studies is provided in Appendix B.

Overall, we identified six eligible studies, reported across 20 articles. Five RCTs provided data on the efficacy of MBRP, and three RCTs provided data on the safety of MBRP; one RCT (Lee, Bowen, and Bai, 2011) met eligibility criteria but reported efficacy data insufficiently to be included in meta-analyses and did not report any safety data. See Table 3.1 for the evidence base for this study's key questions.

Figure 3.1. Flow Diagram of Search Results

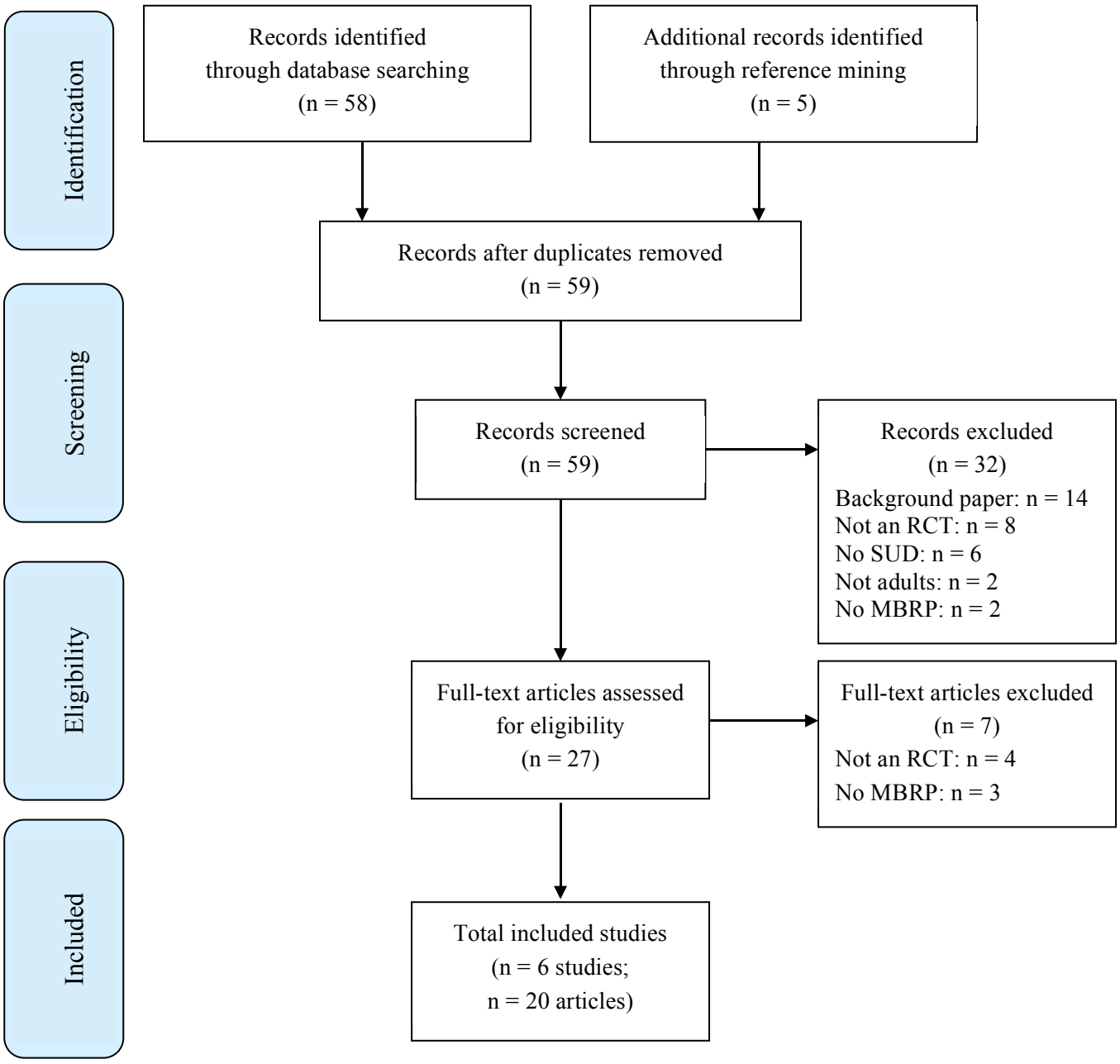


Table 3.1. Evidence Base for Key Questions

Key Question		Number of RCTs
KQ 1	What are the efficacy and safety of mindfulness based relapse prevention (MBRP), as an adjunctive or monotherapy, for adults with alcohol, opioid, stimulant, or cannabis use disorders compared with treatment as usual, waitlists, no treatment, or other active treatments?	• 5 RCTs with efficacy data • 3 RCTs with safety data
KQ 1a	Does the effect of MBRP vary by the substance targeted (i.e., alcohol, opioids, stimulants, or cannabis)?	• 2 RCTs measuring alcohol use • 1 RCT measuring stimulant use
KQ 1b	Does the effect of MBRP differ if MBRP is offered as an adjunctive therapy rather than as a monotherapy?	• 2 adjunctive therapy • 3 monotherapy
KQ 1c	Does the effect of MBRP on substance use disorders depend on the comparator?	• 3 TAU • 3 active comparator

For Key Question 1a on the effect of MBRP by substance targeted, we identified two RCTs providing information on alcohol use specifically (Bowen et al., 2014; Brewer et al., 2009), and one RCT on stimulant use (Brewer et al., 2009); no RCTs provided information about opioid or cannabis use specifically.

For Key Question 1b on the effect of MBRP as an adjunctive versus a monotherapy, we identified two RCTs providing data on MBRP as an adjunctive therapy (Uhlig, 2009; Witkiewitz et al., 2014), and three RCTs providing data on MBRP as a monotherapy (Bowen et al., 2009; Bowen et al., 2014; Brewer et al., 2009).

For Key Question 1c on the effect of MBRP dependent on type of comparator, we identified 3 RCTs providing data on MBRP versus an active comparator (Bowen et al., 2014; Brewer et al., 2009; Witkiewitz et al., 2014), and three RCTs provided data on MBRP versus treatment as usual (TAU) (Bowen et al., 2009; Bowen et al., 2014; Uhlig, 2009).

Description of Included Studies

Design. All RCTs randomized individual participants rather than clusters of participants (see Table 3.2). Overall, studies assigned 685 participants, ranging in size from 24 participants in one RCT (Lee, Bowen, and Bai, 2011) to 286 participants in another (Bowen, Witkiewitz, Clifasefi, et al., 2014), with a median sample size of 86 participants per study. Two studies did not report any information about a power calculation (Bowen, Witkiewitz, Clifasefi, et al., 2014; Brewer et al., 2009), one study reported an *a priori* power calculation with targeted sample size achieved (Uhlig, 2009), and three studies noted a post hoc analysis indicating insufficient power (Bowen, Chawla, et al., 2009; Lee, Bowen, and Bai, 2011; Witkiewitz et al., 2014). One study was reported in a dissertation that did not undergo formal peer review (Uhlig, 2009).

Setting. Five studies took place in the United States (Bowen, Chawla, et al., 2009; Bowen, Witkiewitz, Clifasefi, et al., 2014; Brewer et al., 2009; Uhlig, 2009; Witkiewitz et al., 2014), and one study took place in Taiwan (Lee, Bowen, and Bai, 2011). All studies took place in SUD specialty care settings, with two studies taking place in SUD specialty care within prison settings (Lee, Bowen, and Bai, 2011; Witkiewitz et al., 2014). One study took place at two different sites (Bowen, Witkiewitz, Clifasefi, et al., 2014), while the rest were single-site studies. One RCT evaluated MBRP during residential care (Witkiewitz et al., 2014), whereas four RCTs evaluated MBRP after care (Bowen, Chawla, et al., 2009; Bowen, Witkiewitz, Clifasefi, et al., 2014; Brewer et al., 2009; Uhlig, 2009).

Participants. Average age ranged between 35.8 and 40.7 years old. One RCT had only females (Witkiewitz et al., 2014), and another had only males (Lee, Bowen, and Bai, 2011); of the remaining four RCTs, the proportion of males ranged from 63.7 percent to 72.7 percent. No study restricted participants by primary substance of abuse, with participants using various substances such as alcohol, cocaine, methamphetamines, opiates, and cannabis. All studies but one (Witkiewitz et al., 2014) excluded participants with other mental health disorders.

Interventions. The total length of MBRP ranged from 8 to 16 hours of intervention sessions; all RCTs involved MBRP in a group setting. Two RCTs by the program developers reported using manualized MBRP with no adaptations, involving eight weekly two-hour sessions (Bowen, Chawla, et al., 2009; Bowen, Witkiewitz, Clifasefi, et al., 2014). The four other RCTs evaluated a shortened version of MBRP that differed in number, length, focus, and frequency of sessions (Brewer et al., 2009; Lee, Bowen, and Bai, 2011; Uhlig, 2009; Witkiewitz et al., 2014). Two RCTs reported co-interventions delivered alongside MBRP: One provided MBRP training in addition to the Matrix Model (Uhlig, 2009), and another exposed participants (in both the MBRP and comparison group) to multiple other treatment programs during their residential treatment stay (Witkiewitz et al., 2014).

Table 3.2. Evidence Table of Included Studies

Study Details	Participants	Intervention/Treatment	Outcomes/Results
Parent study: Bowen, Chawla, et al., 2009 **References**: Bowen, Chawla, et al., 2009; Bowen and Kurz, 2012; Chawla et al., 2010; Chawla 2011; Collins et al., 2009; Grow et al., 2015; Hsu, Collins, and Marlatt, 2013; Witkiewitz and Bowen, 2010 **Country:** United States **Study design:** Individually randomized controlled trial **Purpose:** Evaluate feasibility and efficacy of MBRP versus TAU **Quality rating:** Poor High attrition rate (30% attrition), no use of intention-to-treat analysis, do not report all outcomes collected, baseline imbalance in race	**Number of patients:** 168 (93 MBRP, 75 TAU) **Baseline substance use:** Primary substances of abuse were alcohol (45.2%), cocaine/crack (36.2%), methamphetamines (13.7%), opiates/heroin (7.1%), marijuana (5.4%), and other (1.9%). Approximately 19.1% reported polysubstance use. **Comorbid psychological/behavioral health conditions:** None reported **Age (Years):** 40.5 (SD 10.3) **Gender:** 63.7% male **Inclusion criteria:** Recruited from a private, nonprofit agency providing a continuum of care for alcohol and drug use disorders. Between the ages of 18 and 70, fluent in English, had completed intensive outpatient or inpatient treatment in the previous 2 weeks, and were medically cleared for participation **Exclusion criteria:** Psychosis, dementia, imminent suicide risk, significant withdrawal risk, or need for more intensive treatment	**Content of MBRP intervention:** Manualized MBRP in group setting **Health care setting:** Outpatient SUD specialty care **Number of sites:** 1 **Dosage:** 2-hour weekly sessions over 8 weeks (16 hours total) **Timing of intervention administration:** Aftercare **Co-interventions:** None reported **Comparator:** TAU. Standard outpatient aftercare provided by agency; maintain abstinence through a 12-step-process–oriented format: discussed rational thinking skills, grief/loss, assertiveness, self-esteem, goal setting, interpersonal relations experience. Relapse prevention skills were included in some of the groups. Groups lasted approximately 1.5 hours and met 1–2 times weekly. Therapists were licensed chemical dependency counselors, with varying levels of experience. **Primary endpoint:** Frequency of substance use (follow-up not specified) **Power calculation:** Insufficient power (post hoc analysis) **Follow-up:** 4 months	**Relapse:** Any drug days of drug use at 4-month follow-up: OR 0.98 (CI 0.50 to 1.91), p > .05 (favors MBRP) **Frequency of substance use:** Alcohol or other drug use days over the past 60 days, using TLFB • Postintervention: SMD −0.42 (CI −0.77 to −0.08), p < 0.05 (favors MBRP) • 2-month follow-up: SMD −0.30 (CI −0.65 to 0.05), p > 0.05 (favors MBRP) • 4-month follow-up: SMD 0.00 (CI −0.37 to 0.37), p > 0.05 (no difference) **Withdrawal/craving symptoms:** Scores on Penn Alcohol Craving Scale (PACS), adapted for substance use generally • Postintervention: SMD −0.49 (CI −0.89 to −0.09), p < 0.05 (favors MBRP) • 2-month follow-up: SMD −0.32 (CI −0.73 to 0.09), p > 0.05 (favors MBRP) • 4-month follow-up: SMD −0.14 (CI −0.50 to 0.22), p > 0.05 (favors MBRP) **Recovery outcomes:** 3 participants in the TAU group were incarcerated at 4 months **Functional status:** Depression symptoms, as measured by the Beck Depression Inventory • Postintervention: SMD −0.16 (CI −0.50 to 0.19), p > 0.05 (favors MBRP) Negative consequences, as measured by the Short Inventory of Problems Scale (SIPS): • Postintervention: SMD −0.22 (CI −0.61 to 0.17), p > 0.05 (favors MBRP) • 2-month follow-up: SMD −0.16 (CI −0.57 to 0.24), p > 0.05 (favors MBRP) • 4-month follow-up: SMD −0.14 (CI −0.50 to 0.21), p > 0.05 (favors MBRP) **Adverse events:** No adverse events reported

Study Details	Participants	Intervention/Treatment	Outcomes/Results
Parent study: Bowen, Witkiewitz, Clifasefi, et al., 2014 **References:** Bowen, Witkiewitz, Clifasefi, et al., 2014; Bowen, and Enkema, 2014; Carroll, 2014; Douglas, Shilling, and Lustyk, 2012; Grow, 2014; Lustyk, Douglas, and Shilling, 2012 **Country:** United States **Study design:** Individually randomized controlled trial **Purpose:** Evaluate the long-term efficacy of MBRP in reducing relapse versus relapse prevention (RP) and TAU over 12-month follow-up **Quality rating:** Fair High attrition rate (27–33% attrition) though used intention-to-treat analysis, comparable groups at baseline, some important outcomes not in report	**Number of patients:** 286 (103 MBRP, 88 RP, 95 TAU) **Baseline substance use:** Alcohol use only: 16 (15.5%) in MBRP sample, 9 (10.2%) in RP sample, and 14 (14.7%) in TAU sample. Polysubstance use: 81 (78.6%) in MBRP sample, 75 (85.2%) in RP sample, and 79 (83.2%) in TAU sample. Abstinence at baseline: 41 (41.6%) in MBRP sample, 32 (37.2%) in RP sample, and 29 (30.5%) in TAU sample. **Comorbid psychological/behavioral health conditions:** Severity of Dependence Scale at baseline (mean): 9.52 (SD 4.23) for MBRP, 10.27 (SD 3.67) for RP, and 8.52 (SD 4.43) for TAU. Current psychotic disorder or dementia part of exclusion criteria. **Age (Years):** Range of 18–70 years old. Per condition: MBRP 39.1 (SD 10.9); RP 38.9 (SD 10.9); TAU 37.2 (SD 10.8). **Gender:** 71.5% male **Inclusion criteria:** Age 18 years or older, English fluency, medical clearance, ability to attend treatment sessions, agreement to random assignment and follow-up assessments, completion of initial intensive outpatient or inpatient care	**Content of MBRP intervention:** Manualized MBRP in group setting **Health care setting:** Outpatient SUD specialty care **Number of sites:** 2 **Dosage:** 2-hour weekly sessions over 8 weeks (16 hours total) **Timing of intervention administration:** Aftercare **Co-interventions:** None reported **Comparator 1:** Relapse prevention (RP). RP matched MBRP in time, format, size, location, and scope of assigned homework. Primary objectives included assessment of high-risk situations, cognitive and behavioral coping skills, problem solving, goal setting, self-efficacy, and social support. Participants monitored daily craving and mood. **Comparator 2:** Treatment as usual (TAU). TAU was abstinence based, primarily process oriented, and based on the Alcoholics/Narcotics Anonymous 12-step program. Weekly groups included facilitated recovery-oriented discussions in an open-group format; groups met 1 to 2 times weekly for 1.5 hours. TAU participants remained in standard aftercare alongside individuals not enrolled in the study. **Primary endpoint:** Frequency of substance use and relapse at 12-month follow-up **Power calculation:** None reported	**Relapse:** Any drug use in the past 90 days, using TLFB • MBRP versus RP, 3 months: OR 1.01 (CI 0.43 to 2.38), p > .05 (favors RP) • MBRP versus TAU, 3 months: OR 0.45 (CI 0.21 to 0.98), p < .05 (favors MBRP) • MBRP versus RP, 6 months: OR 1.14 (CI 0.41 to 3.18), p > .05 (favors RP) • MBRP versus TAU, 6 months: OR 0.30 (CI 0.13 to 0.70), p < .05 (favors MBRP) • MBRP versus RP, 12 months: OR 0.42 (CI 0.17 to 1.04), p > .05 (favors MBRP) • MBRP versus TAU, 12 months: OR 0.50 (CI 0.20 to 1.27), p > .05 (favors MBRP) Any heavy drinking in the past 90 days, using TLFB • MBRP versus RP, 3-month follow-up: OR 0.46 (CI 0.20 to 1.02), p > .05 (favors MBRP) • MBRP versus TAU, 3-month follow-up: OR 0.41 (CI 0.18 to 0.91), p < .05 (favors MBRP) • MBRP versus RP, 6-month follow-up: OR 0.77 (CI 0.27 to 2.16), p > .05 (favors MBRP) • MBRP versus TAU, 6-month follow-up: OR 0.35 (CI 0.14 to 0.88), p < .05 (favors MBRP) • MBRP versus RP, 12-month follow-up: OR 0.27 (CI 0.11 to 0.66), p < .05 (favors MBRP) • MBRP versus TAU, 12-month follow-up: OR 0.31 (CI 0.12 to 0.78), p < .05 (favors MBRP) **Frequency of substance use:** Number of days spent using drugs in the past 90 days, using TLFB • MBRP versus RP, 3-month follow-up: SMD 0.13 (CI −0.18 to 0.44), p > .05 (favors RP) • MBRP versus TAU, 3-month follow-up: SMD −0.08 (CI −0.39 to 0.23), p > .05 (favors MBRP) • MBRP versus RP, 6-month follow-up: SMD 0.09 (CI −0.23 to 0.41), p > .05 (favors RP) • MBRP versus TAU, 6-month follow-up: SMD −0.20 (CI −0.52 to 0.13), p > .05 (favors MBRP) • MBRP versus RP, 12-month follow-up: SMD −0.18 (CI −0.51 to 0.15), p > .05 (favors MBRP) • MBRP versus TAU, 12-month follow-up: SMD −0.10 (CI −0.43 to 0.23), p > .05 (favors MBRP)

Study Details	Participants	Intervention/Treatment	Outcomes/Results
	Exclusion criteria: Current psychotic disorder, dementia, suicidality, imminent danger to others, participation in previous MBRP trials	**Follow-up:** 12 months	Number of days spent heavy drinking in past 90 days, using TLFB • MBRP versus RP, 3-month follow-up: SMD −0.02 (CI −0.33 to 0.29), p > .05 (favors MBRP) • MBRP versus TAU, 3-month follow-up: SMD −0.07 (CI −0.38 to 0.24), p > .05 (favors MBRP) • MBRP versus RP, 6-month follow-up: SMD 0.07 (CI −0.25 to 0.39), p > .05 (favors RP) • MBRP versus TAU, 6-month follow-up: SMD −0.11 (CI −0.43 to 0.22), p > .05 (favors MBRP) • MBRP versus RP, 12-month follow-up: SMD −0.27 (CI −0.61 to 0.05), p > .05 (favors MBRP) • MBRP versus TAU, 12-month follow-up: SMD −0.25 (CI −0.58 to 0.08), p > .05 (favors MBRP) **Treatment drop-out:** • MBRP versus RP: OR 0.63 (CI 0.14 to 2.89), p > .05 (favors MBRP) • MBRP versus TAU: OR 0.92 (CI 0.18 to 4.67), p > .05 (favors MBRP) **Recovery outcomes:** Incarceration at 6 months • MBRP versus RP: risk ratio (RR) 0.85 (CI 0.20 to 3.72), p > .05 (favors RP) • MBRP versus TAU: RR 0.82 (CI 0.19 to 3.57), p > .05 (favors TAU) **Adverse events:** 1 participant in Comparator 1 (relapse prevention) died during the 12-month follow-up 1 participant in MBRP enrolled as an inpatient at 6 months

Study Details	Participants	Intervention/Treatment	Outcomes/Results
Parent study: Brewer et al., 2009 **References:** Brewer et al., 2009 **Country:** United States **Study design:** Individually randomized controlled trial **Purpose:** Assess MBRP versus cognitive behavioral therapy (CBT) on substance use and treatment acceptability **Quality rating:** Poor High attrition (61% attrition), no use of intention-to-treat analysis, baseline imbalance in marital status	**Number of patients:** 36 (21 MBRP, 15 CBT) **Baseline substance use:** DSM-IV criteria for alcohol dependence (68%) and cocaine dependence (48%). 3 participants (15%) positive for marijuana, and 3 participants (15%) positive for cocaine at baseline. Average days of use over 28 days before baseline: Alcohol: 0.05 (SD 0.21); Marijuana: 0.14 (SD 0.36); Cocaine: 0.05 (SD 0.21); Tobacco: 0.45 (SD 0.51); Average number of lifetime drug treatments: 2 (SD 2.1). **Comorbid psychological/behavioral health conditions:** None reported **Age (Years):** 38.2 (SD 11.9) **Gender:** 72% male **Inclusion criteria:** Seeking treatment at a community-based outpatient treatment facility, English-speaking adults who met DSM-IV criteria for alcohol and/or cocaine abuse/dependence in the past year **Exclusion criteria:** Under age 18, currently at clinically significant risk for suicide or homicide, had a current psychotic disorder (assessed by a psychiatrist), had a cognitive impairment precluding completion of study-related activities, were on beta-blocker treatment	**Content of MBRP intervention:** Shortened version of MBRP in a group setting. Sessions were divided into two 4-week modules that could be completed in either order. Yoga meditation was removed. Weekly sessions were shortened to approximately one hour, primarily by shortening the guided meditation exercises. **Health care setting:** Outpatient SUD specialty care **Number of sites:** 1 **Dosage:** 1-hour weekly sessions over 9 weeks (9 hours total) **Timing of intervention administration:** Aftercare **Co-interventions:** None reported **Comparator:** Cognitive behavioral therapy (CBT). CBT was delivered over a 12-week period using the National Institute on Drug Abuse CBT manual. Sessions were delivered weekly in a continuous fashion such that individuals could enter treatment based on a weekly rolling admission process. Each session lasted roughly 1 hour. Groups were capped at 8 persons to ensure optimal treatment settings. **Primary endpoint:** None reported **Power calculation:** None reported **Follow-up:** Postintervention	**Relapse:** N/A **Frequency of substance use:** Number of days of alcohol use in the past 28 days: SMD 0.99 (CI −0.16 to 2.15), p > .05 (favors CBT) Number of days of cocaine use in the past 28 days: SMD 0.77 (CI −0.36 to 1.90), p > .05 (favors CBT) **Treatment dropout:** OR 0.67 (CI 0.17 to 2.65), p > .05 (favors MBRP) **Functional status:** Anxiety, measured by the Differential Emotion Scale (DES) Anxious Sub-Scale scores • Postintervention: SMD −1.42 (CI −2.64 to −0.21), p < 0.05 (favors MBRP) **Adverse events:** No adverse events reported

Study Details	Participants	Intervention/Treatment	Outcomes/Results
Parent study: Lee, Bowen, and Bai, 2011 **References:** Lee, Bowen, and Bai, 2011 **Country:** Taiwan **Study design:** Individually randomized controlled trial **Purpose:** Examine the effectiveness of MBRP on psychosocial outcomes among incarcerated illicit drug users who were currently abstinent from illicit drugs **Quality rating:** Poor Small baseline imbalance in drug use before incarceration (though all had been abstinent for at least 6 months), not all important outcomes were considered, no outcome was reported sufficiently for use in meta-analysis	**Number of patients:** 24 (10 MBRP, 14 TAU) **Baseline substance use:** All participants had used illicit drugs in the past and had been abstinent from illicit drugs for 6 months or more. MBRP participants used drugs less frequently before incarceration compared with those in TAU. **Comorbid psychological/behavioral health conditions:** None reported **Age (Years):** 40.7 **Gender:** 100% male **Inclusion criteria:** Participants had 1-year sentences due to possession or sale of illicit drugs. All participants had used illicit drugs in the past and had been abstinent from illicit drugs for 6 months or more **Exclusion criteria:** Individuals with psychotic features, delirium, or illiteracy were excluded from the study	**Content of MBRP intervention:** Shortened, more-frequent version of MBRP in a group setting **Health care setting:** SUD specialty care in prison **Number of sites:** 1 **Dosage:** 90-minute weekly sessions over 10 weeks (15 hours total) **Timing of intervention administration:** During residential care in prison **Co-interventions:** None reported **Comparator:** Treatment as usual (TAU). TAU involved substance use education. **Primary endpoint:** None reported **Power calculation:** Insufficient power (post hoc analysis) **Follow-up:** Postintervention	**Relapse:** N/A **Functional status:** Depression symptoms, measured by the Beck Depression Inventory • Postintervention: MBRP participant average score of 4.5 (SD 1.48) **Adverse events:** N/A

Study Details	Participants	Intervention/Treatment	Outcomes/Results
Parent study: Uhlig, 2009 **References:** Uhlig, 2009 **Country:** United States **Study design:** Individually randomized controlled trial **Purpose:** Determine effectiveness of MBRP + TAU (Matrix Model) versus TAU (Matrix Model) on coping skills, motivation, attendance, and abstinence **Quality rating:** Poor High attrition (30–50% attrition), no use of intention-to-treat analysis, important outcomes missing	**Number of patients:** 66 (33 MBRP, 33 TAU) **Baseline substance use:** Substance dependence: Alcohol: 66.7%; cocaine: 19.7%; opiates: 4.5%; sedatives: 3.0%; cannabis: 6.1% A majority (66.7%) of the population sample had been less than 30 days' sober **Comorbid psychological/behavioral health conditions:** None reported **Age (Years):** 18–22 years: 4.5%; 23–29: 19.7%; 30–39: 25.8%; 40–49: 21.2%; 50–59: 24.2%; > 59: 4.5% **Gender:** 72.7% male **Inclusion criteria:** 18 years or older, sober at the time of the study, willing to participate and learn meditation, ability to commit to participate for the duration of the 4-week study, no hospitalizations for mental illness in the past **Exclusion criteria:** Not in age range, not being sober at the time of the study, demonstrating an unwillingness to be a part of the MBRP group, not being committed to participation in the full 4-week program, history of hospitalization for mental illness	**Content of MBRP intervention:** Adapted to a 4-week time frame due to extremely high dropout rate of up to 50% observed by clinical supervisors, worksite limitations, and an outpatient emphasis. Lectures were supplemented by a compact disk (CD). MBRP administered in a group setting. **Health care setting:** Outpatient SUD specialty care **Number of sites:** 1 **Dosage:** 2-hour weekly sessions over 4 weeks (8 hours total) **Timing of intervention administration:** Aftercare **Co-interventions:** Yes—MBRP training in addition to the Matrix Model **Comparator:** TAU, which was the Matrix Model at this center. This model focuses on external social interaction and external measurement of success (i.e., urine toxicology). Involves 8–32 weeks of psycho-education, family education, social support, and individual counseling combined with weekly urine testing and optional 12-step meetings. **Primary endpoint:** None reported **Power calculation:** *A priori* power calculation; targeted sample size achieved **Follow-up:** Postintervention	**Relapse:** Negative toxicology rates (proportion of negative screens over total screens) at postintervention: OR 0.49 (CI 0.20 to 1.18), p > .05 (favors MBRP) **Adverse events:** N/A

Study Details	Participants	Intervention/Treatment	Outcomes/Results
Parent study: Witkiewitz et al., 2014 **References:** Witkiewitz, Greenfield, and Bowen, 2013; Witkiewitz et al., 2014 **Country:** United States **Study design:** Individually randomized controlled trial **Purpose:** Determine whether MBRP is a feasible and effective intervention, compared with relapse prevention (RP), in the prevention of substance use relapse during intensive residential substance abuse treatment for women referred from the criminal-justice system **Quality rating:** Fair High attrition rate (40% attrition), use of intention-to-treat analysis	**Number of patients:** 105 (55 MBRP, 50 RP) **Baseline substance use:** Methamphetamine: 35.5%; heroin/opiates: 22.6%; cocaine: 19.4%; alcohol: 9.7%; marijuana: 6.5%; nicotine: 3.2%; other drugs: 3.2% **Comorbid psychological/behavioral health conditions:** A portion of the sample (n = 86; 81.9%) indicated that 46% of the women had at least one suicide attempt; 69.2% endorsed a severe trauma; 70.7% reported chronic depression; 73.5% reported anxiety; and 89.2% reported history of verbal, emotional, or physical abuse **Age (Years):** MBRP: 35.8 (SD 9.5), RP: 32.4 (SD 8.9) **Gender:** 0% male **Inclusion criteria:** Residency at the treatment center (previously involved in illegal activities, such as drug use/possession, burglary, and prostitution), proficiency in English, willingness to be randomized to treatment condition, and sufficient self-reported cognitive ability to understand and provide consent **Exclusion criteria:** None reported	**Content of MBRP intervention:** Shortened, more-frequent version of MBRP. Groups had rolling admission. Offered 30-minute meditation sitting groups 4 days per week, providing scheduled time to practice mindfulness exercises. **Health care setting:** Residential SUD specialty care **Number of sites:** 1 **Dosage:** Two 50-minute sessions a week for 8 weeks (13 hours and 20 minutes total) **Timing of intervention administration:** During residential care **Co-interventions:** Yes—participants in both conditions were exposed to multiple other treatment programs during residential treatment stay **Comparator:** RP, based on manual by Daley and Marlatt and portions of the Coping Skills Training Guide. Taught participants to assess high-risk situations for relapse, build coping skills for craving and high-risk situations, and teach skills for problem-solving, goal-setting, drink refusal self-efficacy, social support, and balanced lifestyle. **Primary endpoint:** Frequency of substance use at 3.5 months **Power calculation:** Insufficient power (post hoc analysis) **Follow-up:** 3.5 months	**Relapse:** Number who used drugs in the past 30 days at 3.5-month follow-up: OR 0.16 (CI 0.02 to 1.43), p > .05 (favors MBRP) **Frequency of substance use:** Days of drug use in the past 30 days, using TLFB: SMD −0.36 (CI −0.90 to 0.18), p > .05 (favors MBRP) **Functional status:** Negative consequences, measured by the Short Inventory of Problems Scale (SIPS): • 3.5-month follow-up: SMD −0.45 (CI − 0.99 to 0.09), p > .05 (favors MBRP) Social functioning, measured by the Addiction Severity Index (ASI) Family/Social Problems Subscale • 3.5-month follow-up: SMD −0.07 (CI −0.60 to 0.46), p > 0.05 (favors MBRP) Psychiatric problems, measured by the Addiction Severity Index (ASI) Psychiatric Problems Subscale • 3.5-month follow-up: SMD −0.53 (CI −1.08 to 0.01), p > 0.05 (favors MBRP) **Health-related quality of life:** Medical status, measured by the Addiction Severity Index (ASI) Medical Problems Subscale • 3.5-month follow-up: SMD −0.65 (CI −1.20 to −0.10), p < 0.05 (favors MBRP) **Treatment dropout:** OR 1.47 (CI 0.64 to 3.36), p > .05 (favors RP) **Recovery outcomes:** Legal problems, measured by the Addiction Severity Index (ASI) Legal Problems Subscale • 3.5-month follow-up: SMD −1.20 (CI −1.78 to −0.62), p < 0.05 (favors MBRP) **Adverse events:** N/A

Study Details	Participants	Intervention/Treatment	Outcomes/Results

NOTES: “Not reported” indicates that this information was not provided in study manuscripts but was able to be reported. “None reported” indicates that this information was not provided in study manuscripts, but we do not know whether this information was relevant or collected.
SD = Standard deviation.
N/A = Not applicable.

Comparators. One RCT had three arms: One group received MBRP, and the two comparator groups received either standard relapse prevention or TAU (Bowen, Witkiewitz, Clifasefi, et al., 2014). Two other RCTs employed active comparators: either cognitive behavioral therapy (Brewer et al., 2009) or standard relapse prevention (Witkiewitz et al., 2014). The other RCTs used a TAU comparator, which included either substance use education (Lee, Bowen, and Bai, 2011), the Matrix Model (Uhlig, 2009), or a predominantly 12-step-process–oriented group (Bowen, Chawla, et al., 2009). The Matrix Model involves weekly sessions focusing on external social interaction and external measurement of treatment success, such as urine toxicology. The 12-step-process–oriented program involved standard outpatient aftercare provided by the agency that served as the study site; participants discussed rational thinking skills, grief and loss, assertiveness, self-esteem, goal setting, and experience with interpersonal relations. Groups met one or two times each week, with sessions lasting approximately 1.5 hours.

Outcomes. Length follow-up ranged from immediately postintervention to 12-month postintervention. Four RCTs provided information about relapse (Bowen, Chawla, et al., 2009; Bowen, Witkiewitz, Clifasefi, et al., 2014; Uhlig, 2009; Witkiewitz et al., 2014), four RCTs on frequency of substance use (Bowen, Chawla, et al., 2009; Bowen, Witkiewitz, Clifasefi, et al., 2014; Brewer et al., 2009; Witkiewitz et al., 2014), three RCTs on treatment dropout (Bowen, Witkiewitz, Clifasefi, et al., 2014; Brewer et al., 2009; Witkiewitz et al., 2014), one RCT on withdrawal/craving symptoms (Bowen, Chawla, et al., 2009), three RCTs on recovery outcomes (Bowen, Chawla, et al., 2009; Bowen, Witkiewitz, Clifasefi, et al., 2014; Witkiewitz et al., 2014), three RCTs on functional status (Bowen, Chawla, et al., 2009; Brewer et al., 2009; Witkiewitz et al., 2014), one RCT on health-related quality of life (Witkiewitz et al., 2014), and three RCTs on adverse events (Bowen, Chawla, et al., 2009; Bowen, Witkiewitz, Clifasefi, et al., 2014; Brewer et al., 2009). No RCTs provided information on quantity of substance use. Three RCTs listed frequency of substance use as the primary outcome (Bowen, Chawla, et al., 2009; Bowen, Witkiewitz, Clifasefi, et al., 2014; Witkiewitz et al., 2014), one of which also listed relapse as a co-primary outcome (Bowen, Witkiewitz, Clifasefi, et al., 2014). None of the other RCTs specified primary outcomes.

Study Quality and Risk of Bias for Individual Included Studies

The study quality and risk of bias for each of the individual included studies can be found in Table 3.3. No studies obtained a "good" quality rating. Two studies were judged to be of fair quality: One study had a high attrition rate (27–33 percent), though it used intention-to-treat analysis; had comparable groups at baseline; and was missing some important outcomes (Bowen, Witkiewitz, Clifasefi, et al., 2014). Another study had a high attrition rate (40 percent), though it did use intention-to-treat analysis (Witkiewitz et al., 2014). Four further studies were judged to be of poor quality. One study had a small baseline imbalance in drug use before incarceration (though all participants had been abstinent for at least 6 months), and no outcome was reported

sufficiently for use in meta-analysis (Lee, Bowen, and Bai, 2011). Another study had a high attrition rate (30 percent), did not use intention-to-treat analysis, did not report all outcomes collected, and had significant baseline imbalance (Bowen, Chawla, et al., 2009). Another study also had a very high attrition rate (61 percent), no use of intention-to-treat analysis, and significant baseline imbalance in participant marital status (Brewer et al., 2009). One final study had high attrition (30–50 percent), did not use intention-to-treat analysis, and had important outcomes missing (Uhlig, 2009).

Random sequence generation. Three studies had unclear selection bias because they did not report their method for random sequence generation; three other studies reported adequate methods for random sequence generation (e.g., computerized random number generator).

Allocation concealment. All studies had unclear selection bias because they did not report their allocation concealment method.

Blinding of participants and providers. All studies had "high" risk of performance bias, because it is generally impossible to blind participants and providers to awareness of delivering or receiving the interventions in this study. Given that such blinding is impossible, these ratings will not be used in the GRADE ratings in the summary of findings table.

Blinding of outcome assessors. Four studies had unclear risk of detection bias because they did not report whether outcome assessors were blind to participant intervention conditions. Two studies had low risk of bias because the authors explicitly indicated that the outcome assessors were blind to intervention assignment.

Outcome data. All but one study had high risk of attrition bias, due to significant overall attrition among participants in all intervention groups.

Selective outcome reporting. Two studies had high risk of reporting bias because they did not report all outcome data for measures mentioned in the methods section of the manuscript or a trial registration entry. Four studies had unclear risk of bias because the authors did not provide a protocol for the study or an *a priori* trial registration entry.

Intervention developer. Three studies had direct involvement of one or more intervention developers as trial authors. Authors of the other studies acknowledged the assistance of program developers, though it was unclear whether developers actually were involved in running the RCT.

Table 3.3. Study Quality/Risk of Bias for Individual Included Studies

Study	Random Sequence Generation (selection bias)	Allocation Concealment (selection bias)	Blinding of Participants and Providers (performance bias)	Blinding of Outcome Assessors (detection bias)	Completeness of Reporting Outcome Data (attrition bias)	Selective Outcome Reporting (reporting bias)	Involvement of Intervention Developer in Trial (independent replication)	Other Biases[a]	USPSTF Quality Rating[b]
Bowen, Chawla, et al., 2009	Low	Unclear	High	Unclear	High	High	Yes	Baseline confounding, ITT analysis	Poor
Bowen, Witkiewitz, Clifasefi, et al., 2014	Unclear	Unclear	High	Unclear	High	High	Yes	Baseline confounding	Fair
Brewer et al., 2009	Low	Unclear	High	Low	High	Unclear	Unclear	Baseline confounding, ITT analysis	Poor
Lee, Bowen, and Bai, 2011	Unclear	Unclear	High	Low	Low	High	Yes	Baseline confounding	Poor
Uhlig, 2009	Unclear	Unclear	High	Unclear	High	Unclear	Unclear	Baseline confounding, ITT analysis	Poor
Witkiewitz et al., 2014	Low	Unclear	High	Unclear	High	Unclear	Unclear	Crossovers/ contamination	Fair

NOTES: ITT = intention-to-treat; USPSTF = U.S. Preventive Services Task Force.

[a] Other biases include balance of confounders, crossovers/contamination, measurement, intervention definition, and intention-to-treat analysis.

[b] The USPSTF criteria (U.S. Preventive Services Task Force, 2008) for study quality involve assessment of various factors related to the internal validity of the study. “Good” is the highest ranking, which involves comparable groups with low attrition, with outcomes being reliably and validly measured and analyzed. “Fair” is the next highest rating and involves studies with one or a few potential concerns (e.g., some though not major differences between groups exist at follow-up), though intention-to-treat analysis was performed. “Poor” is the lowest ranking and involves studies with one or more “fatal flaws” (e.g., no intention-to-treat analysis).

KQ 1: What Is the Efficacy and Safety of MBRP, as an Adjunctive or Monotherapy, for Any Substance Use Versus Any Comparator?

We identified five RCTs providing data on the overall efficacy of MBRP (Bowen, Chawla, et al., 2009; Bowen, Witkiewitz, Clifasefi, et al., 2014; Brewer et al., 2009; Uhlig, 2009; Witkiewitz et al., 2014) and three RCTs providing data on the overall safety of MBRP (Bowen, Chawla, et al., 2009; Bowen, Witkiewitz, Clifasefi, et al., 2014; Brewer et al., 2009). Overall, we did not find strong evidence in support of MBRP as an efficacious intervention for SUDs, either as an adjunctive or monotherapy. No significant effects were found for relapse, frequency of substance use, withdrawal/craving symptoms, functional status, or recovery outcomes. We did identify a significant effect in favor of MBRP as an adjunctive therapy (versus standard relapse prevention) for health-related quality of life (SMD −0.65; CI −1.20 to −0.10). However, this was based on very low quality evidence: Results were based on one RCT (Witkiewitz et al., 2014) with only 105 participants (15 percent of randomized participants), with the evidence downgraded for high attrition bias, inability to judge consistency across multiple RCTs, and a wide confidence interval spanning effect sizes with different clinical conclusions. No study provided outcome data on quantity of substance use. Three RCTs reported on adverse events. Two RCTs reported no adverse events (Bowen, Chawla, et al., 2009; Brewer et al., 2009), while the third reported that one participant receiving standard relapse prevention died, and another participant receiving MBRP was admitted to inpatient care for reasons unknown (Bowen, Witkiewitz, Clifasefi, et al., 2014).

In the results sections that follow, we first present results for a given outcome from 0–11 months postintervention and then results from 12 months or more postintervention for that outcome. Our presentation of results focuses on findings from meta-analyses when multiple studies provided data for a particular outcome, though we note when data for a given outcome are from one study only.

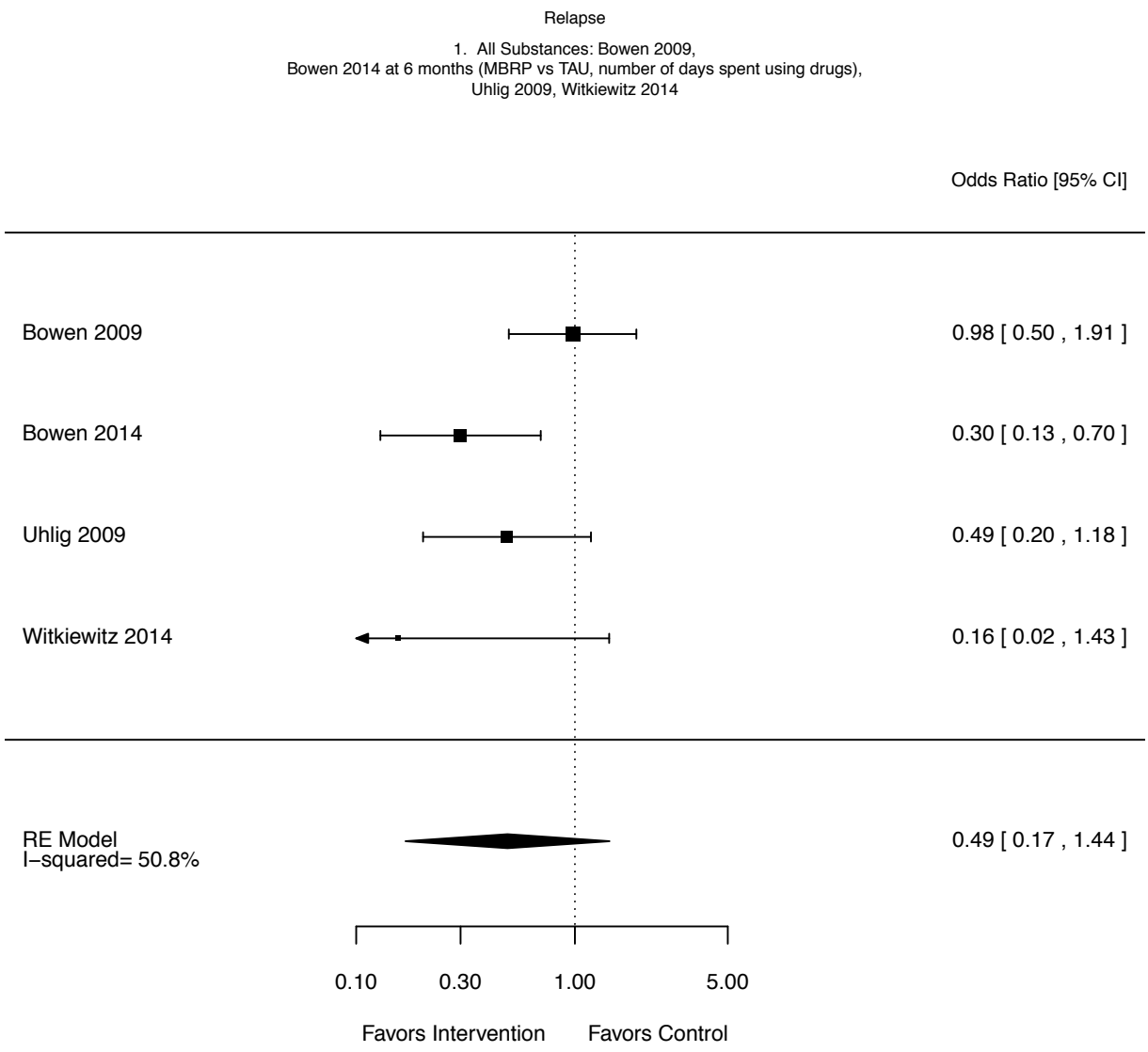
Relapse

Four RCTs (Bowen, Chawla, et al., 2009; Bowen, Witkiewitz, Clifasefi, et al., 2014; Uhlig, 2009; Witkiewitz et al., 2014) with 625 participants (91 percent of randomized participants) reported relapse data, either as any days of drug use or as positive toxicology rates. When pooled across all studies reporting relapse data, there was very low quality evidence of no statistically significant difference between MBRP as an adjunctive therapy or a monotherapy (versus TAU or standard relapse prevention) up to six-month follow-up, with moderate heterogeneity (OR 0.49; CI 0.17 to 1.44; I^2 50.8%; see Figure 3.2). This effect estimate did not substantially differ when using data from Bowen, Witkiewitz, Clifasefi, et al. (2014) at three-month follow-up, using standard relapse prevention as the comparator rather than TAU for Bowen, Witkiewitz, Clifasefi, et al. (2014), and using data from Bowen, Witkiewitz, Clifasefi, et al. (2014) on number of heavy

drinking days rather than days spent using drugs.

One study provided data on relapse at 12-month follow-up (Bowen, Witkiewitz, Clifasefi, et al., 2014). Assessments of relapse to any drug use in the 90 days prior to 12-month follow-up yielded no evidence of an effect when MBRP as a monotherapy was compared with TAU (OR 0.50; CI 0.20 to 1.27) or standard relapse prevention (OR 0.42; CI 0.17 to 1.04). Significant effects were found for MBRP as a monotherapy on relapse to any heavy drinking of alcohol in the 90 days prior to 12-month follow-up with TAU (OR 0.31; CI 0.12 to 0.78) or standard relapse prevention (OR 0.27; CI 0.11 to 0.66) as the comparator. This study also reported analyses (controlling for treatment group, age, treatment site, treatment history, treatment hours, and baseline severity of substance dependence) yielding a clinically small effect in favor of standard relapse prevention (versus MBRP as a monotherapy) delaying the time to first day of drug use (hazard ratio [HR] 1.21; CI 1.10 to 1.33), with no evidence of effect on time to first day of heavy drinking (HR 0.72; CI 0.91 to 1.15).

Figure 3.2. MBRP Versus Any Comparator on Substance Use Relapse



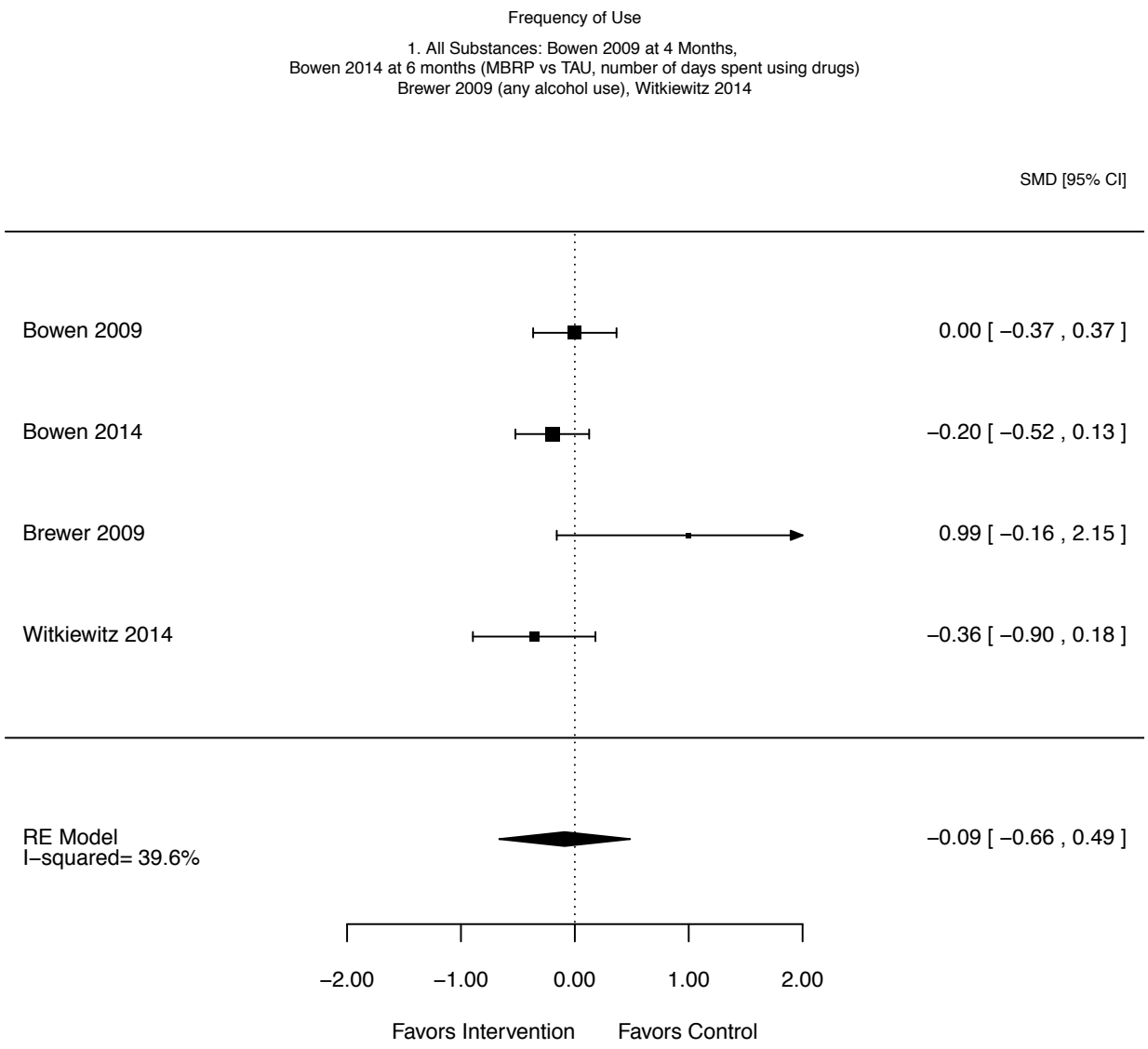
Frequency of Substance Use

Four RCTs (Bowen, Chawla, et al., 2009; Bowen, Witkiewitz, Clifasefi, et al., 2014; Brewer et al., 2009; Witkiewitz et al., 2014) with 595 participants (87 percent of randomized participants) reported frequency of substance use data on number of days of substance use. There was very low quality evidence of no statistically significant difference of MBRP as an adjunctive therapy or a monotherapy (versus standard relapse prevention, cognitive behavioral therapy, or TAU) up to six-month follow-up (SMD −0.09; CI −0.66 to 0.49; see Figure 3.3), and these results were moderately heterogeneous (I^2 39.6%). This effect estimate did not differ when using data from Brewer et al. (2009) on any cocaine use rather than any alcohol use; using data from Bowen, Witkiewitz, Clifasefi, et al. (2014) at three-month rather than at six-month follow-up; using standard relapse prevention as the comparator in Bowen, Witkiewitz, Clifasefi, et al.

(2014) rather than TAU; using data from Bowen, Witkiewitz, Clifasefi, et al. (2014) on heavy drinking days rather than days spent using any drug; and using data from Bowen, Chawla, et al. (2009) at postintervention or two-month follow-up.

One study provided data on frequency of substance use at 12-month follow-up (Bowen, Witkiewitz, Clifasefi, et al., 2014). Assessments of any drug use in the 90 days prior to 12-month follow-up yielded no evidence of an effect when MBRP as a monotherapy was compared with TAU (SMD −0.10; CI −0.43 to 0.23) or relapse prevention (SMD −0.18; CI −0.51 to 0.15). Similar results were found for any heavy drinking in the 90 days prior to 12-month follow-up with standard relapse prevention (SMD −0.27; CI −0.61 to 0.05) or TAU (SMD −0.25; CI −0.58 to 0.08) as comparator.

Figure 3.3. MBRP Versus Any Comparator on Frequency of Substance Use



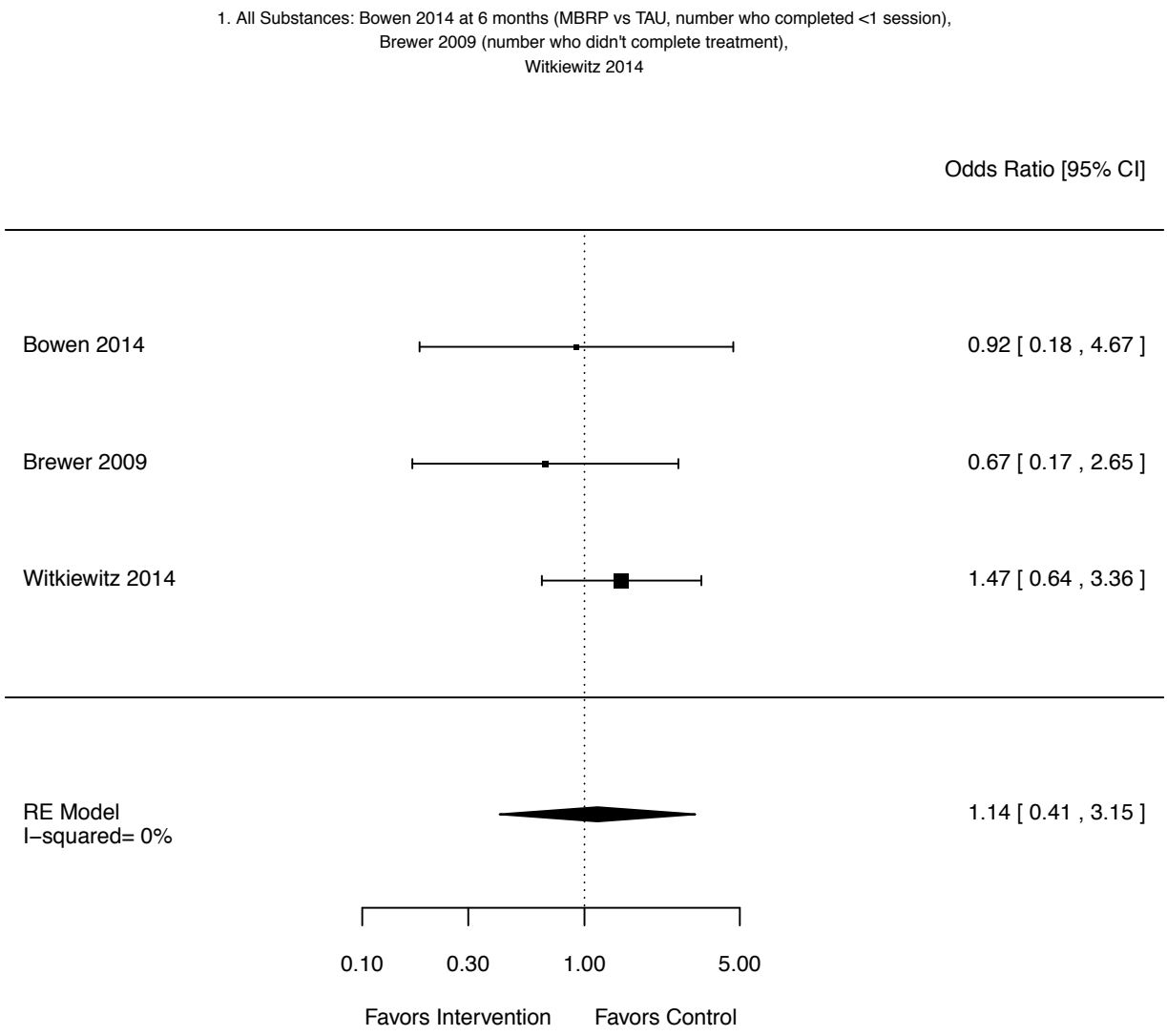
Withdrawal/Craving Symptoms

One RCT (Bowen, Chawla, et al., 2009) with 168 participants (25 percent of randomized participants) reported withdrawal/craving symptoms data, using the Penn Alcohol Craving Scale, adapted for substance use generally. There was very low quality evidence of a clinically moderate difference in favor of MBRP as a monotherapy versus TAU at postintervention (SMD −0.49; CI −0.89 to −0.09), though there was no effect at two-month follow-up (SMD −0.32; CI −0.73 to 0.09) and four-month follow-up (SMD −0.14; CI −0.50 to 0.22).

Treatment Dropout

Three RCTs (Bowen, Witkiewitz, Clifasefi, et al., 2014; Brewer et al., 2009; Witkiewitz et al., 2014) with 427 participants (62 percent of randomized participants) reported treatment dropout data, either as number who completed treatment or number who completed less than one session. There was low quality evidence of no significant difference between MBRP as a monotherapy or adjunctive therapy (versus any comparator: standard relapse prevention, cognitive behavioral therapy, or TAU) at postintervention (OR 1.14; CI 0.41 to 3.15; I^2 0%; see Figure 3.4). This effect estimate did not differ when removing Bowen, Witkiewitz, Clifasefi, et al. (2014), which reported number who completed less than one session rather than the number completing treatment; when using Bowen, Witkiewitz, Clifasefi, et al. (2014) data on number who did not attend the first session, rather than the number who completed less than one session; when using standard relapse prevention as the comparison group rather than TAU from Bowen, Witkiewitz, Clifasefi, et al. (2014); and when using number who did not initiate treatment in Brewer et al. (2009), rather than number who did not complete treatment.

Figure 3.4. MBRP Versus Any Comparator on Treatment Dropout



Health-Related Quality of Life

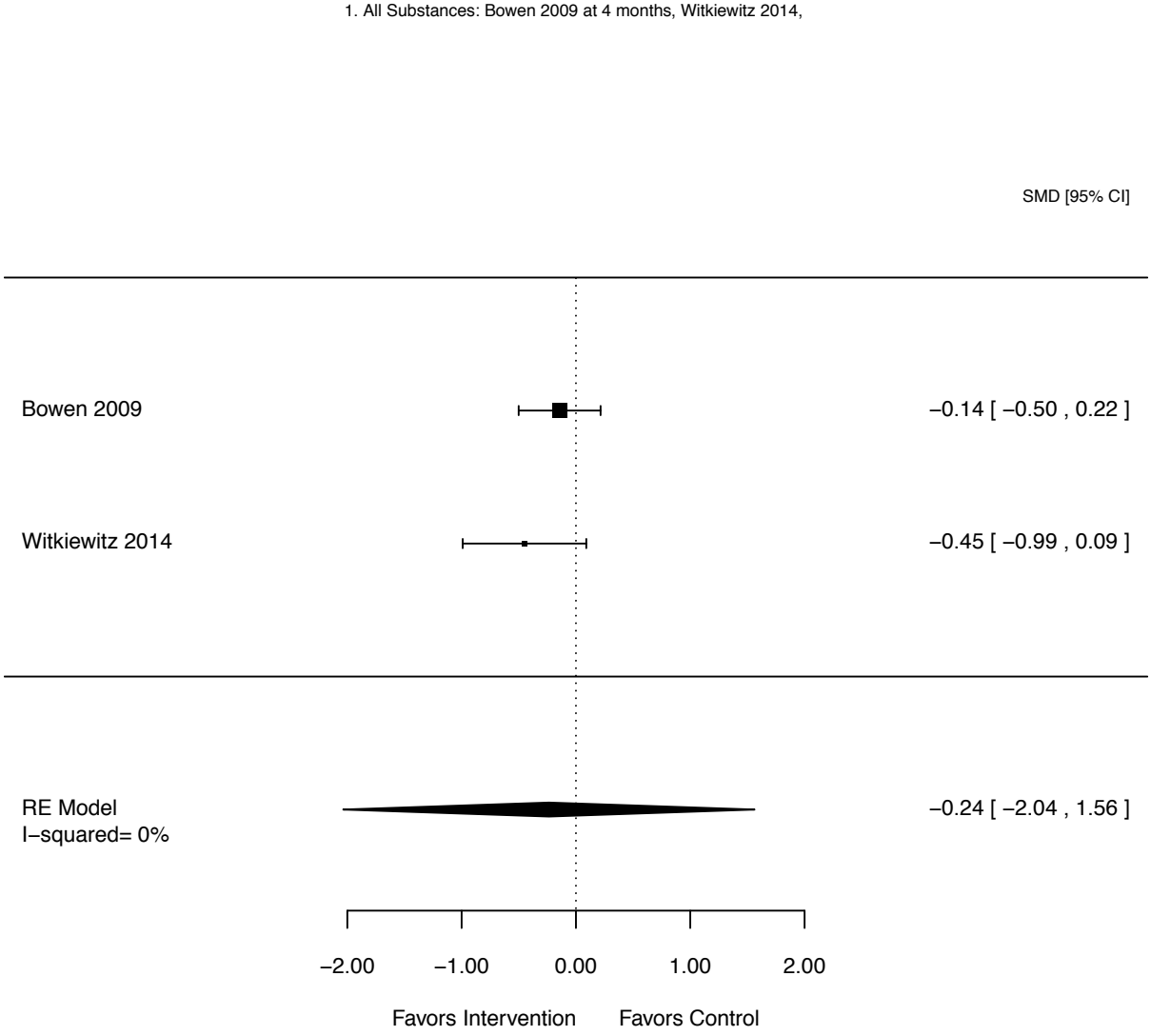
One RCT (Witkiewitz et al., 2014) with 105 participants (15 percent of randomized participants) reported health-related quality of life data, measured by the Addiction Severity Index Medical Problems subscale. There was very low quality evidence (due to attrition bias, inconsistency, and imprecision) of a clinically moderate effect in favor of MBRP (as an adjunctive therapy) versus standard relapse prevention at 3.5-month follow-up (SMD −0.65; CI −1.20 to −0.10).

Functional Status

Two RCTs (Bowen, Chawla, et al., 2009; Witkiewitz et al., 2014) with 273 participants (40 percent of randomized participants) reported functional status data on negative consequences of drug use, measured by the Short Inventory of Problems scale. There was low quality evidence of no significant effect for MBRP as an adjunctive or monotherapy (versus standard relapse prevention or TAU) up to four-month follow-up (pooled SMD −0.24; CI −2.04 to 1.56; I^2 0%; Bowen, Chawla, et al., 2009: SMD −0.14, CI −0.50 to 0.22; Witkiewitz et al., 2014: SMD −0.45, CI −0.99 to 0.09; see Figure 3.5). This effect estimate did not differ when using data from Bowen, Chawla, et al. (2009) at postintervention or at two-month follow-up.

One RCT also measured depressive symptoms using the Beck Depression Inventory (Bowen, Chawla, et al., 2009), yielding no evidence of an effect of MBRP (as a monotherapy) versus TAU at postintervention (SMD −0.16; CI −0.50 to 0.19). Another RCT assessed anxiety using the Differential Emotion Scale Anxious subscale scores (Brewer et al., 2009), showing a clinically large effect in favor of MBRP (as a monotherapy) versus cognitive behavioral therapy at postintervention (SMD −1.42; CI −2.64 to −0.21). An additional RCT measured social functioning using the Addiction Severity Index (ASI) Family/Social Problems subscale (Witkiewitz et al., 2014), finding no evidence of effect of MBRP (as an adjunctive therapy) versus standard relapse prevention at 3.5-month follow-up (SMD −0.07; CI −0.60 to 0.46). This RCT also measured psychiatric problems, finding no evidence of effect at 3.5-month follow-up (SMD −0.53; CI −1.08 to 0.01).

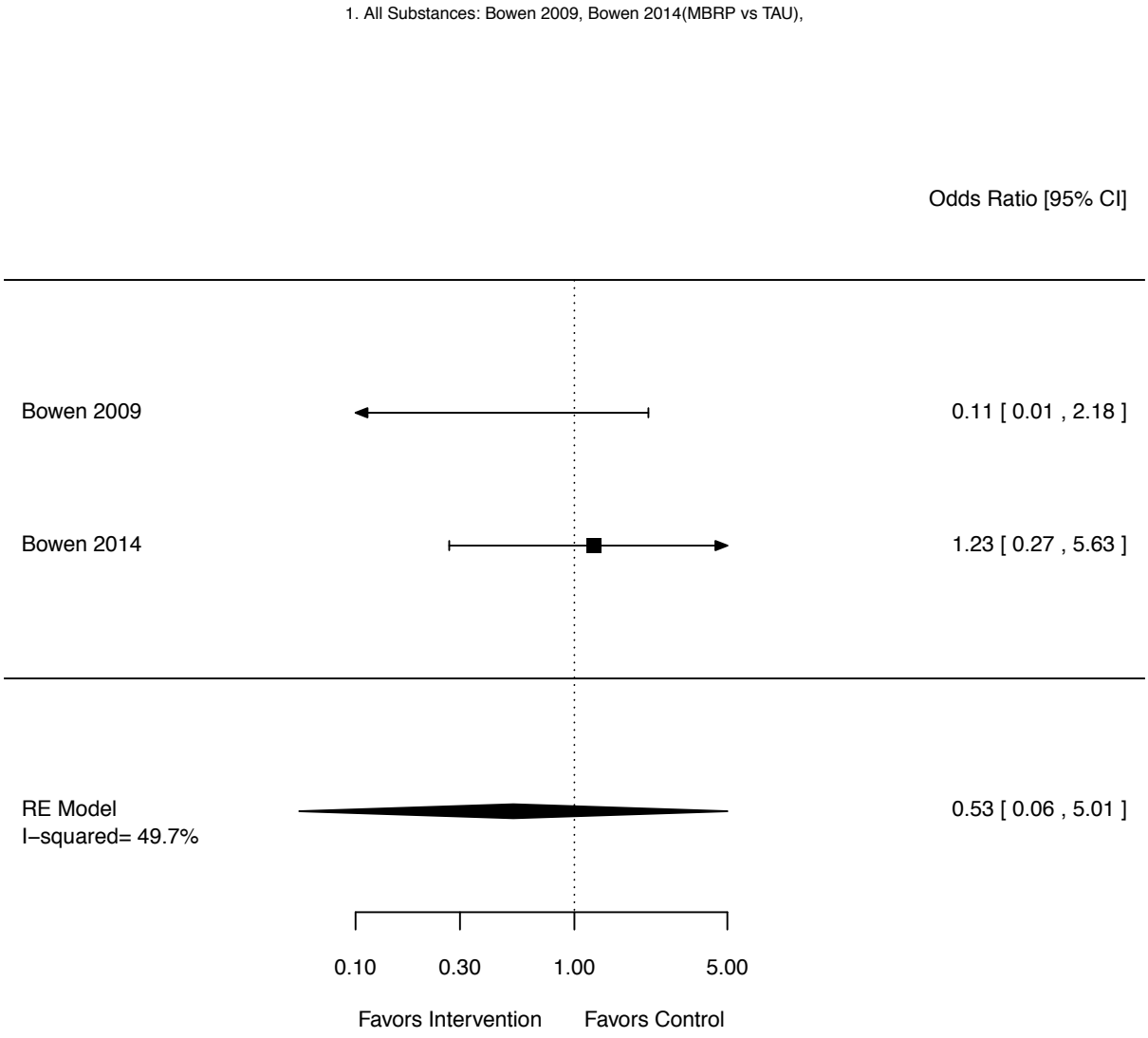
Figure 3.5. MBRP Versus Any Comparator on Functional Status



Recovery Outcomes

Two RCTs with 454 participants (66 percent of randomized participants) reported data on number of participants incarcerated (Bowen, Chawla, et al., 2009; Bowen, Witkiewitz, Clifasefi, et al., 2014). There was very low quality of evidence of no effect of MBRP (as a monotherapy) versus TAU up to six-month follow-up, with moderate heterogeneity (OR 0.53; CI 0.06 to 5.01; I^2 49.7%; Bowen, Chawla, et al., 2009: OR 0.11; CI 0.01 to 2.18; Bowen, Witkiewitz, Clifasefi, et al., 2014: OR 1.23, CI 0.27 to 5.63; see Figure 3.6). This effect estimate did not differ when using standard relapse prevention as the comparator rather than TAU from Bowen, Witkiewitz, Clifasefi, et al. (2014). One RCT also provided information about legal problems using the Addiction Severity Index Legal Problems subscale (Witkiewitz et al., 2014), showing a clinically large effect in favor of MBRP (as an adjunctive therapy) versus standard relapse prevention at 3.5-month follow-up (SMD −1.20; CI −1.78 to −0.62).

Figure 3.6. MBRP Versus Any Comparator on Recovery Outcomes (Incarceration)



Adverse Events

Three RCTs (Bowen, Chawla, et al., 2009; Bowen, Witkiewitz, Clifasefi, et al., 2014; Brewer et al., 2009) with 490 participants (72 percent of randomized participants) reported information about adverse events. Two RCTs indicated that no adverse events were reported (Bowen, Chawla, et al., 2009; Brewer et al., 2009). Another RCT indicated that one participant receiving standard relapse prevention died during the 12-month follow-up, and at six-month follow-up, another participant receiving MBRP as a monotherapy was admitted to inpatient care for reasons unknown (Bowen, Witkiewitz, Clifasefi, et al., 2014).

KQ 1a: Does the Effect of MBRP Vary by the Substance Targeted (i.e., Alcohol, Opioids, Stimulants, or Cannabis)?

All trials involved polysubstance using samples. Of these, only two RCTs provided information on alcohol use specifically (Bowen, Chawla, et al., 2009; Brewer et al., 2009) and one RCT on stimulant use (Brewer et al., 2009). No RCT provided information about opioid or cannabis use specifically. We did not find any direct comparisons of MBRP for one substance versus another. We found no evidence of effect of MBRP for relapse to alcohol use, frequency of alcohol use, and frequency of stimulant use.

Alcohol Use

There was very low quality of evidence from one RCT (Bowen, Witkiewitz, Clifasefi, et al., 2014) of a statistically significant effect on relapse to alcohol use for MBRP (as a monotherapy) versus TAU at six-month follow-up (OR 0.35; CI 0.14 to 0.88). This estimate did not differ when looking at three-month follow-up or 12-month follow-up. Effects were not statistically significant when using standard relapse prevention as the comparator or looking at time to first heavy drinking day.

There was very low quality evidence from two RCTs (Bowen, Witkiewitz, Clifasefi, et al., 2014; Brewer et al., 2009) of no significant effect on frequency of alcohol use for MBRP as a monotherapy (versus cognitive behavioral therapy or TAU) at six-month follow-up (pooled SMD 0.30; CI −6.45 to 7.05; Bowen, Witkiewitz, Clifasefi, et al., 2014: SMD −0.11; CI −0.43 to 0.22; Brewer et al., 2009: SMD 0.99, CI −0.16 to 2.15), and these results were substantially heterogeneous (I^2 69.2%). This estimate did not differ when using standard relapse prevention as the comparator in Bowen, Witkiewitz, Clifasefi, et al. (2014), using three-month follow-up for Bowen, Witkiewitz, Clifasefi, et al. (2014), and assessing any heavy drinking in the 90 days prior to 12-month follow-up for MBRP versus standard relapse prevention or TAU as the comparator.

Stimulant Use

There was very low quality evidence from one RCT (Brewer et al., 2009) of no statistically significant effect on frequency of cocaine use for MBRP (as a monotherapy) versus cognitive behavioral therapy at postintervention (SMD 0.77; CI −0.36 to 1.90).

KQ 1b: Does the Effect of MBRP Differ If MBRP Is Offered as an Adjunctive Therapy Rather Than as a Monotherapy?

Three RCTs provided data on MBRP as a monotherapy (Bowen, Chawla, et al., 2009; Bowen, Witkiewitz, Clifasefi, et al., 2014; Brewer et al., 2009), and two RCTs provided data on MBRP as an adjunctive therapy (Uhlig, 2009; Witkiewitz et al., 2014). In one RCT, TAU (the Matrix Model) was compared with MBRP plus TAU (Uhlig, 2009). In another RCT, participants

in both the MBRP and the active comparator (standard relapse prevention) conditions were exposed to multiple other unnamed treatment programs during their residential treatment stay (Witkiewitz et al., 2014).

We found no studies that compared MBRP as a monotherapy with MBRP as an adjunctive therapy. We consequently conducted an indirect comparison of the results of analyses of MBRP as a monotherapy (versus comparator interventions) and MBRP as an adjunctive therapy (versus comparator interventions). We did not find any evidence of effect of MBRP as a monotherapy for any outcomes. As mentioned, MBRP plus TAU (versus TAU) had more-favorable outcomes for health-related quality of life (SMD −0.65; CI −1.20 to −0.10) and legal problems (SMD −1.20; CI −1.78 to −0.62), though this quality of evidence was very low and is based on the results of one moderately sized RCT with all females in a prison setting (Witkiewitz et al., 2014). Moreover, there was no evidence of effect of MBRP plus any adjunctive therapy versus any comparator for substance use relapse, frequency of substance use, treatment dropout, and functional status.

Mindfulness-Based Relapse Prevention as a Monotherapy

There was very low quality evidence from two RCTs (Bowen, Chawla, et al., 2009; Bowen, Witkiewitz, Clifasefi, et al., 2014) of no effect on relapse to any substance use for MBRP (as a monotherapy) versus TAU up to six-month follow-up (pooled OR 0.56; CI 0.00 to 992.23; I^2 78.2%; Bowen, Chawla, et al., 2009: OR 0.98; CI 0.50 to 1.91; Bowen, Witkiewitz, Clifasefi, et al., 2014: OR 0.30; CI 0.13 to 0.70). This effect estimate did not differ when using three-month follow-up data from Bowen, Witkiewitz, Clifasefi, et al. (2014) or data on relapse to any heavy drinking rather than any drug use from Bowen, Witkiewitz, Clifasefi, et al. (2014). There was also no statistically significant effect of MBRP (as a monotherapy) versus TAU on relapse to any substance use at 12-month follow-up with either TAU (OR 0.50; CI 0.20 to 1.27) or standard relapse prevention (OR 0.42; CI 0.17 to 1.04) as the comparator. As mentioned, there was a clinically small effect in favor of standard relapse prevention (versus MBRP as a monotherapy) delaying the time to first day of drug use (HR 1.21; CI 1.10 to 1.33), with no evidence of effect on time to first heavy drinking day. Significant effects were also found in favor of MBRP (as a monotherapy) for relapse to any heavy drinking in the 90 days prior to 12-month follow-up with TAU (OR 0.31; CI 0.12 to 0.78) or standard relapse prevention (OR 0.27; CI 0.11 to 0.66) as the comparator.

There was low quality evidence from two RCTs (Bowen, Chawla, et al., 2009; Bowen, Witkiewitz, Clifasefi, et al., 2014) of no effect on frequency of substance use for MBRP (as a monotherapy) versus TAU up to six-month follow-up (pooled SMD −0.11; CI −1.36 to 1.14; I^2 0%; Bowen, Chawla, et al., 2009: SMD 0.00; CI −0.37 to 0.37; Bowen, Witkiewitz, Clifasefi, et al., 2014: SMD −0.20; CI −0.52 to 0.13). This effect estimate did not differ when using data from Bowen, Witkiewitz, Clifasefi, et al. (2014) at three-month follow-up; using data from Bowen, Witkiewitz, Clifasefi, et al. (2014) on days spent heavy drinking; and using data from

Bowen, Chawla, et al. (2009) at postintervention or two-month follow-up. There was also no statistically significant effect on any drug use or on any heavy drinking in the 90 days prior to 12-month follow-up (Bowen, Witkiewitz, Clifasefi, et al., 2014).

As mentioned in the discussion about KQ 1, there was very low quality evidence from one RCT (Bowen, Chawla, et al., 2009) of a clinically moderate effect on withdrawal/craving in favor of MBRP as a monotherapy (versus TAU) at postintervention (SMD −0.49; CI −0.89 to −0.09), though there was no effect at two-month follow-up (SMD −0.32; CI −0.73 to 0.09) or four-month follow-up (SMD −0.14; CI −0.50 to 0.22).

There was low quality evidence from two RCTs (Bowen, Witkiewitz, Clifasefi, et al., 2014; Brewer et al., 2009) of no significant effect on treatment dropout for MBRP as a monotherapy (versus cognitive behavioral therapy or TAU) at postintervention (OR 0.76; CI 0.27 to 2.18; I^2 0%; Bowen, Witkiewitz, Clifasefi, et al., 2014: OR 0.92; CI 0.18 to 4.67; Brewer et al., 2009: OR 0.67; CI 0.17 to 2.65). This effect estimate did not differ when using number who did not attend the first session from Bowen, Witkiewitz, Clifasefi, et al. (2014) and using number who did not initiate treatment from Brewer et al. (2009). However, there was a statistically significant effect in favor of MBRP when using standard relapse prevention data from Bowen, Witkiewitz, Clifasefi, et al. (2014) (OR 0.65; CI 0.45 to 0.93; I^2 0%; Bowen, Witkiewitz, Clifasefi, et al., 2014: OR 0.63; CI 0.14 to 2.89).

There was very low quality evidence from one RCT (Bowen, Chawla, et al., 2009) of no significant effect on functional status for MBRP as a monotherapy versus TAU at four-month follow-up (SMD −0.14; CI −0.50 to 0.22), with a similar finding for postintervention (SMD −0.22; CI −0.61 to 0.17) and at two-month follow-up (SMD −0.16; CI −0.57 to 0.24).

As mentioned in the discussion about KQ 1, there was very low quality evidence from two RCTs (Bowen, Chawla, et al., 2009; Bowen, Witkiewitz, Clifasefi, et al., 2014) of no effect on number of participants incarcerated for MBRP as a monotherapy versus TAU up to six-month follow-up (OR 0.53; CI 0.06 to 5.01; I^2 49.7%).

Mindfulness-Based Relapse Prevention as an Adjunctive Therapy

There was low quality evidence from two RCTs (Uhlig, 2009; Witkiewitz et al., 2014) of no statistically significant difference in relapse to any substance use for MBRP with any adjunctive therapy (versus standard relapse prevention or TAU) up to 3.5-month follow-up (pooled OR 0.42; CI 0.00 to 62.17; I^2 0%; Uhlig, 2009: OR 0.49; CI 0.20 to 2.18; Witkiewitz et al., 2014: OR 0.16; CI 0.02 to 1.43).

Based on results from one RCT (Witkiewitz et al., 2014), there was very low quality evidence of no effect of MBRP (as an adjunct to other treatments) versus standard relapse prevention at 3.5-month follow-up on frequency of drug use (SMD −0.36; CI −0.90 to 0.18), treatment dropout (OR 1.47; CI 0.64 to 3.36), and functional status (SMD −0.45; CI − 0.99 to 0.09). As mentioned, this RCT also reported a positive effect for health-related quality of life (SMD −0.65; CI −1.20 to −0.10) and legal problems (SMD −1.20; CI −1.78 to −0.62).

KQ 1c: Does the Effect of MBRP on SUDs Depend on the Comparator?

Two RCTs provided data on MBRP versus an active comparator (Brewer et al., 2009; Witkiewitz et al., 2014), and two RCTs compared MBRP and specific TAU interventions (Bowen, Chawla, et al., 2009; Uhlig, 2009). An additional trial compared MBRP with TAU, yet it did not provide information on outcomes of interest to this review (Lee, Bowen and Bai, 2011). One RCT had both an active comparator and a TAU comparator involving a 12-step-process–oriented group intervention (Bowen, Witkiewitz, Clifasefi, et al., 2014). In total, then, data were provided on MBRP versus active comparators in three trials and on MBRP versus TAU in three trials. Active comparators included weekly group-based cognitive behavioral therapy (Brewer et al., 2009) and standard relapse prevention (Bowen, Witkiewitz, Clifasefi, et al., 2014). TAU included weekly 12-step-process–oriented groups (Bowen, Chawla, et al., 2009; Bowen, Witkiewitz, Clifasefi, et al., 2014) and the Matrix Model (Uhlig, 2009). One RCT involved both intervention arms receiving TAU (Uhlig, 2009).

Across studies, there was no indication of effects differing by the comparator used in the identified studies, because across all studies, no positive effects were found for MBRP compared with either TAU or with active comparators, except for the aforementioned effect in favor of MBRP as an adjunctive therapy versus standard relapse prevention for health-related quality of life (SMD −0.65, CI −1.20 to −0.10). However, we did not identify data on health-related quality of life comparing MBRP and TAU.

Mindfulness-Based Relapse Prevention Versus Treatment as Usual

Based on data from three RCTs (Bowen, Chawla, et al., 2009; Bowen, Witkiewitz, Clifasefi, et al., 2014; Uhlig, 2009), there was very low quality evidence of no significant difference on relapse to any substance use for MBRP (as a monotherapy or an adjunctive therapy) versus TAU (i.e., groups based on 12-step processes and the Matrix Model) up to six-month follow-up, with moderate heterogeneity (OR 0.54; CI 0.12 to 2.46; I^2 78.2%). This effect estimate did not substantially differ when using data at three-month follow-up from Bowen, Witkiewitz, Clifasefi, et al. (2014); using data from Bowen, Witkiewitz, Clifasefi, et al. (2014) on number of heavy drinking days; and assessing relapse to any drug use in the 90 days prior to 12-month follow-up. There were statistically significant effects from one RCT (Bowen, Witkiewitz, Clifasefi, et al., 2014) when assessing any heavy drinking in the 90 days prior to 12-month follow-up (OR 0.31; CI 0.12 to 0.78).

There was low quality evidence from two RCTs (Bowen, Chawla, et al., 2009; Bowen, Witkiewitz, Clifasefi, et al., 2014) of no effect on frequency of substance use for MBRP (as a monotherapy) versus TAU up to six-month follow-up (pooled SMD −0.11; CI −0.14 to 0.35; I^2 0%; Bowen, Chawla, et al., 2009: SMD 0.00; CI −0.37 to 0.37; Bowen, Witkiewitz, Clifasefi, et al., 2014: SMD −0.20; CI −0.52 to 0.13). This effect estimate did not differ when using data from Bowen, Witkiewitz, Clifasefi, et al. (2014) at three-month follow-up; using data from

Bowen, Witkiewitz, Clifasefi, et al. (2014) on heavy drinking days; using data from Bowen, Chawla, et al. (2009) at postintervention or two-month follow-up; and assessing any drug use or any heavy drinking in the 90 days prior to 12-month follow-up.

As mentioned, there was very low quality evidence from one RCT (Bowen, Chawla, et al., 2009) of a clinically moderate effect on withdrawal/craving in favor of MBRP (as a monotherapy) versus TAU at postintervention (SMD −0.49; CI −0.89 to −0.09), though this clinical effect was not statistically significant at two-month follow-up (SMD −0.32; CI −0.73 to 0.09) and four-month follow-up (SMD −0.14; CI −0.50 to 0.22).

There was very low quality evidence from one RCT (Bowen, Witkiewitz, Clifasefi, et al., 2014) of no significant effect on treatment dropout for MBRP (as a monotherapy) versus TAU using either the number of participants who completed less than one session (OR 0.92; CI 0.18 to 4.67) or the number of participants who attended the first session (OR 0.97; CI 0.52 to 1.81).

As mentioned in the discussion about KQ 1b, there was very low quality evidence from one RCT (Bowen, Chawla, et al., 2009) of no significant effect on functional status for MBRP (as a monotherapy) versus TAU at four-month follow-up (SMD −0.14; CI −0.50 to 0.21), with similar findings at postintervention and two-month follow-up.

As mentioned in the discussion about KQ 1, there was very low quality evidence from two RCTs (Bowen, Chawla, et al., 2009; Bowen, Witkiewitz, Clifasefi, et al., 2014) of no significant effect on recovery outcomes for MBRP (as a monotherapy) versus TAU up to six-month follow-up, with moderate heterogeneity (OR 0.53; CI 0.06 to 5.01; I^2 49.7%).

Mindfulness-Based Relapse Prevention Versus Active Comparator

There was very low quality evidence from two RCTs (Bowen, Witkiewitz, Clifasefi, et al., 2014; Witkiewitz et al., 2014) of no significant effect on relapse to any drug use for MBRP (as a monotherapy or adjunctive therapy) versus standard relapse prevention up to six-month follow-up, with considerable heterogeneity (pooled OR 0.54; CI 0.00 to 119,992.24; I^2 60.8%; Bowen, Witkiewitz, Clifasefi, et al., 2014: OR 1.14; CI 0.41 to 3.18; Witkiewitz et al., 2014: OR 0.16; CI 0.02 to 1.43). This effect estimate did not differ when using data at three-month follow-up from Bowen, Witkiewitz, Clifasefi, et al. (2014); using data from Bowen, Witkiewitz, Clifasefi, et al. (2014) on number of days spent heavy drinking; assessing relapse to any drug use in the 90 days prior to 12-month follow-up (OR 0.42; CI 0.17 to 1.04), and assessing time to first day of heavy drinking (HR 0.72; CI 0.91 to 1.15). As mentioned, there was evidence from one study (Bowen, Witkiewitz, Clifasefi, et al., 2014) of a clinically small effect in favor of standard relapse prevention (versus MBRP as a monotherapy) delaying the time to first day of drug use (HR 1.21; CI 1.1 to 1.33). Significant effects were found in one RCT (Bowen, Witkiewitz, Clifasefi, et al., 2014) for MBRP (as a monotherapy) versus standard relapse prevention on relapse to any heavy drinking in the 90 days prior to 12-month follow-up (OR 0.27; CI 0.11 to 0.66).

There was very low quality evidence from three RCTs (Bowen, Witkiewitz, Clifasefi, et al., 2014; Brewer et al., 2009; Witkiewitz et al., 2014) of no significant effect on frequency of

substance use for MBRP (as a monotherapy or adjunctive therapy) versus any active comparator up to six-month follow-up, with substantial heterogeneity (SMD 0.06; CI −1.28 to 1.41; I^2 58.4%). This effect estimate did not differ when using any cocaine use from Brewer et al., 2009; using data from Bowen, Witkiewitz, Clifasefi, et al. (2014) at three months; using data from Bowen, Witkiewitz, Clifasefi, et al. (2014) on heavy drinking days; and assessing any drug use or any heavy drinking in the 90 days prior to 12-month follow-up.

As mentioned in the discussion about KQ 1, there was low quality evidence from three RCTs (Bowen, Witkiewitz, Clifasefi, et al., 2014; Brewer et al., 2009; Witkiewitz et al., 2014) of no significant effect on treatment dropout for MBRP (as a monotherapy or adjunctive therapy) versus any active comparator up to six-month follow-up (OR 1.06; CI 0.32 to 3.59; I^2 0%). In addition, there was very low quality evidence of a clinically moderate effect on health-related quality of life in favor of MBRP (as an adjunctive therapy) versus standard relapse prevention (SMD −0.65; CI −1.20 to −0.10) based on data from one RCT (Witkiewitz et al., 2014).

As mentioned in the discussion about KQ 1b, there was very low quality evidence of no significant effect on functional status for MBRP (as an adjunctive therapy) versus standard relapse prevention (SMD −0.45; CI − 0.99 to 0.09), based on data from one RCT (Witkiewitz et al., 2014).

- There was very low quality evidence from one RCT (Bowen, Chawla, et al., 2009) of statistically significant effect on recovery outcomes for MBRP (as a monotherapy) versus standard relapse prevention at six-month follow-up (OR 0.11; CI 0.01 to 2.18).

Chapter Four: Discussion

Summary of Findings

Overall, the available evidence in support of MBRP is very limited. There were no consistent differences between MBRP and any of the comparators for substance use outcomes; moreover, the number of available studies is small, and the quality of this evidence is very low according to strength of evidence assessments using the GRADE approach. One study did not report any outcome data sufficiently for inclusion in meta-analysis (Lee, Bowen, and Bai, 2011). The available evidence on adverse events is also very limited; two RCTs reported no adverse events, while the third reported that one participant receiving standard relapse prevention died, and another participant receiving MBRP was admitted to inpatient care for reasons unknown. However, it is possible that adverse events occurred in the three studies that did not address adverse events in their reports. There were statistically significant effects for MBRP as an adjunctive therapy for health-related quality of life and legal problems, yet this was based on very low quality of evidence from one RCT. Given the quality of evidence, there is uncertainty in the magnitude or stability of effect estimates. See Table 4.1 for a summary of findings and the quality of evidence for this review, organized by key question.

Table 4.1. Quality of Evidence and Summary of Findings

Outcome	Study Design (number of RCTs and participants)	Findings (direction and magnitude of effect)[a]	Study Limitations (study quality; risk of bias)	Inconsistency	Indirectness	Imprecision	GRADE of Evidence for Outcome
KQ 1: MBRP versus any comparator for substance use							
Substance use relapse	4 RCTs, 625 participants	OR 0.49 (CI 0.17 to 1.44), not significant	Downgrade 1[b]	Downgrade 1[f]	Direct	Downgrade 1[h]	Very Low
Frequency of substance use	4 RCTs, 595 participants	SMD −0.09 (CI −0.66 to 0.49), not significant	Downgrade 1[b]	Downgrade 1[f]	Direct	Downgrade 1[h]	Very Low
Withdrawal/craving symptoms	1 RCT, 168 participants	SMD −0.14 (CI −0.50 to 0.22), not significant	Downgrade 1[b,c]	Downgrade 1[g]	Direct	Downgrade 1[h]	Very Low
Treatment dropout	3 RCTs, 427 participants	OR 1.14 (CI 0.41 to 3.15), not significant	Downgrade 1[b,d]	Consistent	Direct	Downgrade 1[h]	Low
Health-related quality of life	1 RCT, 105 participants	SMD −0.65 (CI −1.20 to −0.10), in favor of MBRP compared with relapse prevention	Downgrade 1[b]	Downgrade 1[g]	Direct	Downgrade 1[h]	Very Low
Functional status	2 RCTs, 273 participants	SMD −0.24 (CI −2.04 to 1.56), not significant	Downgrade 1[b]	Consistent	Direct	Downgrade 1[h]	Low
Recovery outcomes	2 RCTs, 454 participants	OR 0.53 (CI 0.06 to 5.01), not significant	Downgrade 1[b,c]	Downgrade 1[f]	Direct	Downgrade 1[h]	Very low
KQ 1a: MBRP versus any comparator for alcohol use							
Alcohol use relapse	1 RCT, 286 participants	OR 0.35 (CI 0.14 to 0.88), in favor of MBRP compared with TAU	Downgrade 1[b]	Downgrade 1[g]	Direct	Downgrade 1[h]	Very Low
Frequency of alcohol use	2 RCTs, 304 participants	SMD 0.30 (CI −6.45 to 7.05), not significant	Downgrade 1[b]	Downgrade 1[f]	Direct	Downgrade 1[h]	Very Low
KQ 1a: MBRP versus any comparator for stimulant use							
Frequency of stimulant use	1 RCT, 36 participants	SMD 0.77 (CI −0.36 to 1.90), not significant	Downgrade 1[b,d,e]	Downgrade 1[g]	Direct	Downgrade 1[h]	Very Low

Outcome	Study Design (number of RCTs and participants)	Findings (direction and magnitude of effect)[a]	Study Limitations (study quality; risk of bias)	Inconsistency	Indirectness	Imprecision	GRADE of Evidence for Outcome
KQ 1b: MBRP as a monotherapy versus any comparator							
Substance use relapse	2 RCTs, 454 participants	OR 0.56 (CI 0.00 to 992.23), not significant	Downgrade 1[b]	Downgrade 1[f]	Direct	Downgrade 1[h]	Very low
Frequency of substance use	3 RCTs, 490 participants	SMD 0.00 (CI −1.03 to 1.03), not significant	Downgrade 1[b]	Downgrade 1[f]	Direct	Downgrade 1[h]	Very low
Withdrawal/craving symptoms	1 RCT, 168 participants	SMD −0.14 (CI −0.50 to 0.22), not significant	Downgrade 1[b,c]	Downgrade 1[g]	Direct	Downgrade 1[h]	Very Low
Treatment dropout	2 RCTs, 322 participants	OR 0.76 (CI 0.27 to 2.18), not significant	Downgrade 1[b]	Consistent	Direct	Downgrade 1[h]	Low
Functional status	1 RCT, 168 participants	SMD −0.14 (CI −0.50 to 0.21), not significant	Downgrade 1[b]	Downgrade 1[g]	Direct	Downgrade 1[h]	Very Low
Recovery outcomes	2 RCTs, 454 participants	OR 0.53 (CI 0.06 to 5.01), not significant	Downgrade 1[b,c]	Downgrade 1[f]	Direct	Downgrade 1[h]	Very low
KQ 1b: MBRP as an adjunctive therapy versus any comparator							
Substance use relapse	2 RCTs, 171 participants	OR 0.42 (CI 0.00 to 62.17), not significant	Downgrade 1[b]	Consistent	Direct	Downgrade 1[h]	Low
Frequency of substance use	1 RCT, 105 participants	SMD −0.36 (CI −0.90 to 0.18), not significant	Downgrade 1[b]	Downgrade 1[g]	Direct	Downgrade 1[h]	Very Low
Treatment dropout	1 RCT, 105 participants	OR 1.47 (CI 0.64 to 3.36), not significant	Downgrade 1[b]	Downgrade 1[g]	Direct	Downgrade 1[h]	Very Low
Health-related quality of life	1 RCT, 105 participants	SMD −0.65 (CI −1.20 to −0.10), in favor of MBRP compared with relapse prevention	Downgrade 1[b]	Downgrade 1[g]	Direct	Downgrade 1[h]	Very Low
Functional status	1 RCT, 105 participants	SMD −0.45 (CI −0.99 to 0.09), not significant	Downgrade 1[b]	Downgrade 1[g]	Direct	Downgrade 1[h]	Very Low
Recovery outcomes (legal problems)	1 RCT, 105 participants	SMD −1.20 (CI −1.78 to −0.62), in favor of MBRP compared with relapse prevention	Downgrade 1[b]	Downgrade 1[g]	Direct	Downgrade 1[h]	Very Low

Outcome	Study Design (number of RCTs and participants)	Findings (direction and magnitude of effect)[a]	Study Limitations (study quality; risk of bias)	Inconsistency	Indirectness	Imprecision	GRADE of Evidence for Outcome
KQ 1c: MBRP versus TAU							
Substance use relapse	3 RCTs, 432 participants	OR 0.54 (CI 0.12 to 2.46), not significant	Downgrade 1[b]	Downgrade 1[f]	Direct	Downgrade 1[h]	Very low
Frequency of substance use	2 RCTs, 366 participants	SMD −0.11 (CI −1.36 to 1.14), not significant	Downgrade 1[b]	Consistent	Direct	Downgrade 1[h]	Low
Withdrawal/craving symptoms	1 RCT, 168 participants	SMD −0.14 (CI −0.50 to 0.22), not significant	Downgrade 1[b,c]	Downgrade 1[g]	Direct	Downgrade 1[h]	Very Low
Treatment dropout	1 RCT, 198 participants	OR 0.92 (CI 0.18 to 4.67), not significant	Downgrade 1[b]	Downgrade 1[g]	Direct	Downgrade 1[h]	Very Low
Functional status	1 RCT, 168 participants	SMD −0.14 (CI −0.50 to 0.21), not significant	Downgrade 1[b]	Downgrade 1[g]	Direct	Downgrade 1[h]	Very Low
Recovery outcomes	2 RCTs, 366 participants	OR 0.53 (CI 0.06 to 5.01), not significant	Downgrade 1[b,c]	Downgrade 1[f]	Direct	Downgrade 1[h]	Very low
KQ 1c: MBRP versus active comparators							
Substance use relapse	2 RCTs, 296 participants	OR 0.54 (CI 0.00 to 119,992), not significant	Downgrade 1[b]	Downgrade 1[f]	Direct	Downgrade 1[h]	Very low
Frequency of substance use	3 RCTs, 332 participants	SMD 0.06 (CI −1.28 to 1.41), not significant	Downgrade 1[b]	Downgrade 1[f]	Direct	Downgrade 1[h]	Very Low
Treatment dropout	3 RCTs, 332 participants	OR 1.06 (CI 0.32 to 3.59), not significant	Downgrade 1[b,d]	Consistent	Direct	Downgrade 1[h]	Low
Health-related quality of life	1 RCT, 105 participants	SMD −0.65 (CI −1.20 to −0.10), in favor of MBRP compared with relapse prevention	Downgrade 1[b]	Downgrade 1[g]	Direct	Downgrade 1[h]	Very Low
Functional status	1 RCT, 105 participants	SMD −0.36 (CI −0.90 to 0.18), not significant	Downgrade 1[b]	Downgrade 1[g]	Direct	Downgrade 1[h]	Very Low
Recovery outcomes	1 RCT, 191 participants	OR 0.11 (CI 0.01 to 2.18), not significant	Downgrade 1[b]	Downgrade 1[g]	Direct	Downgrade 1[h]	Very Low

[a] SMDs less than 0 and ORs less than 1 favor MBRP.
[b] High attrition bias.
[c] Selective reporting bias.
[d] Baseline confounding.
[e] Lacks intention-to-treat analysis.
[f] Inconsistent due to substantial heterogeneity.
[g] Cannot judge consistency, as there was only one RCT.
[h] Wide confidence interval spanning effect sizes with different clinical conclusions.

Regarding KQ 1, no statistically significant effects were found for relapse, frequency of substance use, withdrawal/craving symptoms, functional status, or recovery outcomes across all studies; however, CIs for most of these outcomes were very wide, so clinically important effects cannot be excluded. A statistically significant effect in favor of MBRP (as an adjunctive therapy versus standard relapse prevention) on health-related quality of life at 3.5-month follow-up was based on very low quality evidence. Regarding KQ 1a, evidence was insufficient to determine whether MBRP effects differ by type of substance targeted, because most studies involved polysubstance using samples, results of alcohol versus stimulant use did not find effects for either substance, and we did not identify any data on cannabis or opioid use specifically. Regarding KQ 1b, there was no consistent, high quality of evidence to suggest that MBRP offered as a monotherapy versus an adjunctive therapy yields different effects. Regarding KQ 1c, there was no direct evidence of effects differing by identified comparators (cognitive behavioral therapy or standard relapse prevention as active comparators, 12-step-process-oriented groups or the Matrix Model for TAU). Subgroup analyses did not show differences in effects because no statistically significant treatment effects for MBRP were found across all studies in the respective subgroups. An effect in favor of MBRP for health-related quality of life was found in the comparison to standard relapse prevention; however, as noted, this was based on very low quality evidence from one RCT, and there were no data on this outcome for MBRP versus TAU for comparison.

Most outcome data were for short-term follow-up; only one RCT provided data at 12-month follow-up (Bowen, Witkiewitz, Clifasefi, et al., 2014), which was the longest follow-up point in any study. It is also worth noting that this body of evidence suffers from severe attrition bias, likely because this population is hard to retain. Due to low quality of evidence and a limited number of RCTs, our confidence that abovementioned effects favoring MBRP lie close to true effects is limited; further evidence is needed before concluding that the findings are stable or that the effect estimates lie close to true effects.

Other Reviews in This Area

While mindfulness programs may have health benefits more generally (Grossman et al., 2004), this review agrees with other reviews indicating a need for more studies on mindfulness interventions for substance use (Bowen, Witkiewitz, Chawla, et al., 2011; Chiesa and Serretti, 2014). However, these two previous reviews have stronger conclusions in favor of mindfulness interventions for SUDs than the present review. Differences in conclusions may be due to the fact that these previous reviews did not specifically focus on MBRP, draw from only RCT data, or meta-analyze effects from the studies they included. The current review, in applying rigorous systematic review methods, is likely to provide more-reliable estimates of the effects of MBRP because previous reviews on mindfulness interventions for SUDs did not provide summary treatment estimates, even though results varied across both studies and outcome measures

(Hempel et al., 2014). As a result, this review is consistent with previous research (Goyal et al., 2014; Zgierska et al., 2009) indicating that MBRP has the potential to be an efficacious and safe intervention for SUD, yet currently there are not data to suggest that it is statistically significantly more efficacious than relapse prevention or TAU, whether offered as either an adjunctive therapy or a monotherapy.

Strengths and Limitations

This review has several strengths: an *a priori* research design, duplicate study selection and data abstraction of study information, a comprehensive search of electronic databases, inclusion of gray literature (e.g., dissertations or graduate theses), and risk-of-bias assessments and comprehensive assessments for quality of evidence used to formulate review conclusions. However, some limitations are worth noting. First, we focused only on one specific intervention, but other mindfulness interventions may be useful for SUDs (Hempel et al., 2014). Second, we did not contact trial authors for missing data or to obtain other potential studies not identified by the search strategy. In addition, many meta-analyses pool results from only two RCTs, with the Hartung-Knapp-Sidik-Jonkman method for random-effects models yielding substantially enlarged confidence intervals for some of these analyses; in such instances, we provided the results from the individual studies contributing to these analyses, with no instances in which both studies were statistically significant yet the pooled results were not. In addition, sufficient data were not available to conduct sensitivity analyses omitting lower quality studies for major comparisons. Significant heterogeneity also existed for several outcomes, such as relapse, frequency of substance use, and incarceration. Sources of heterogeneity could include population characteristics, differences in settings, and methods of outcome measure, but we again had too few studies to reliably detect sources of heterogeneity. Lastly, the aforementioned attrition biases throughout this evidence also limited confidence in findings.

Implications for Future Research and Practice

To provide firmer conclusions about the efficacy and safety of MBRP, future RCTs on this intervention are needed. Future RCTs should include larger sample sizes (Moher, Dulberg, and Wells, 1994), measure outcomes at longer follow-up periods of at least 12 months (Bowen, Witkiewitz, Clifasefi, et al., 2014), pre-register their protocol and subsequently report all outcomes measured in trial manuscripts (Chan et al., 2013), and provide RCT reports in compliance with guidance from the CONSORT (Consolidated Standards of Reporting Trials) Statement for reporting RCTs (Moher et al., 2010). Researchers may also wish to consider equity issues with regard to MBRP and other mindfulness-based treatments, such as whether there are gender differences in the effects of these interventions (Katz and Toner, 2013).

Practitioners and policymakers may consider MBRP as a possible adjunctive treatment for health-related quality of life and legal problems; however, given that these results were based on

one RCT without replication, there is uncertainty in the magnitude or stability of these effect estimates. Moreover, the overall pattern of the data does not suggest that MBRP is any more efficacious for SUD outcomes than standard SUD treatments currently widely available. To provide firmer conclusions about the efficacy and safety of MBRP, future RCTs on this intervention are needed.

Appendix A: Search Strategy

PubMed

Time Period Covered
1/1/2000-12/9/2014

Search Strategy
"mindfulness based relapse prevention" OR "mindfulness-based relapse prevention" OR "mindful* relapse prevention" OR "mindfulness relapse prevention" OR mbrp
AND
("Substance-Related Disorders"[Mesh] OR cannabis OR marijuana OR marihuana OR cocaine OR heroin OR methamphetamin* OR methadone* OR street drug* OR substance abus* OR substance misus* OR drug abus* OR addict* OR drinking behavior(SAMHSA) OR (chemical AND dependen*) OR
((drug OR drugs OR substance* OR alcohol* OR tranquilizer* OR tranquiliser* OR chemical OR polydrug* OR narcotic* OR opiate* OR opioid* OR psychotropic* OR intoxic* OR non-prescri*)
AND (misuse or abus* or addict* OR illegal OR illicit OR habit* OR withdraw* OR abstinen* OR abstain* OR rehabilitat*))

==========

PsycINFO

Time Period Covered
1/1/2000-12/9/2014

Language:
English

Search Strategy
"mindfulness based relapse prevention" OR "mindfulness-based relapse prevention" OR "mindful* relapse prevention" OR "mindfulness relapse prevention" OR mbrp
AND
(cannabis or marijuana or marihuana or cocaine or heroin or methamphetamin* or methadone OR street drug* or substance abus* or substance misus* or drug abus* or addict* or (chemical and dependen*)) OR ((drug or drugs or substance* or alcohol* or tranquilizer* or tranquiliser* or chemical or polydrug* or narcotic* or opiate* or opioid* or psychotropic* or intoxic* or non-prescri*) AND (misuse or abus* or addict* or illegal or illicit or habit* or withdraw* or abstinen* or abstain* or rehab*))

==========

CINAHL

Time Period Covered
1/1/2000-2/20/2015

Language
English

Search Strategy
"mindfulness based relapse prevention" OR "mindfulness-based relapse prevention" OR "mindful* relapse prevention" OR "mindfulness relapse prevention" OR mbrp
AND
(cannabis or marijuana or marihuana or cocaine or heroin or methamphetamin* or methadone OR street drug* or substance abus* or substance misus* or drug abus* or addict* or (chemical and dependen*)) OR ((drug or drugs or substance* or alcohol* or tranquilizer* or tranquiliser* or chemical or polydrug* or narcotic* or opiate* or opioid* or psychotropic* or intoxic* or non-prescri*) AND (misuse or abus* or addict* or illegal or illicit or habit* or withdraw* or abstinen* or abstain* or rehab*))

==========

Allied and Complementary Medicine Database (AMED)

Time Period Covered
1/1/2000-2/20/2015

Language
English

Search Strategy
ab("mindfulness based relapse prevention" OR "mindfulness-based relapse prevention" OR "mindful* relapse prevention" OR "mindfulness relapse prevention" OR mbrp) OR
ti("mindfulness based relapse prevention" OR "mindfulness-based relapse prevention" OR "mindful* relapse prevention" OR "mindfulness relapse prevention" OR mbrp) OR
su("mindfulness based relapse prevention" OR "mindfulness-based relapse prevention" OR "mindful* relapse prevention" OR "mindfulness relapse prevention" OR mbrp)

==========

Cochrane CENTRAL

Time Period Covered
1/1/2000-2/20/2015

Language
English

Search Strategy
"mindfulness based relapse prevention" or "mindfulness-based relapse prevention" or "mindful* relapse prevention" or "mindfulness relapse prevention" or mbrp:ti,ab,kw
AND
(cannabis or marijuana or marihuana or cocaine or heroin or methamphetamin* or methadone or street drug* or substance abus* or substance misus* or drug abus* or addict* or (chemical and dependen*)):ti,ab,kw OR ((drug or drugs or substance* or alcohol* or tranquilizer* or tranquiliser* or chemical or polydrug* or narcotic* or opiate* or opioid* or psychotropic* or intoxic* or non-prescri*) AND (misuse or abus* or addict* or illegal or illicit or habit* or withdraw* or abstinen* or abstain* or rehab*))

==========

Web of Science Indexes: SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH

Time Period Covered
1/1/2000-1/13/2015

Language
English

Search Strategy
ts=("mindfulness based relapse prevention" OR "mindfulness-based relapse prevention" OR "mindful* relapse prevention" OR "mindfulness relapse prevention" OR mbrp)
AND
(ts=(cannabis or marijuana or marihuana or cocaine or heroin or methamphetamin* or methadone OR street drug* or substance abus* or substance misus* or drug abus* or addict* or (chemical and dependen*)) OR ((ts=(drug or drugs or substance* or alcohol* or tranquilizer* or tranquiliser* or chemical or polydrug* or narcotic* or opiate* or opioid* or psychotropic* or intoxic* or non-prescri*)
AND ts=(misuse or abus* or addict* or illegal or illicit or habit* or withdraw* or abstinen* or abstain* or rehab*))

Appendix B: Excluded Full-Text Articles

Reason Excluded: Not a Parallel RCT

Amaro, H., "Implementing Mindfulness-Based Relapse Prevention in Diverse Populations: Challenges and Future Directions," *Substance Use and Misuse*, Vol. 49, No. 5, 2014, pp. 612–616.

Florida, D., "Pilot Evaluation of 'Third Wave' Modular Group Psychotherapy for Comorbid Clients," *Australian and New Zealand Journal of Psychiatry*, Vol. 48, 2014, pp. 78–79.

Vieten, C., J. A. Astin, R. Buscemi, and G. P. Galloway, "Development of an Acceptance-Based Coping Intervention for Alcohol Dependence Relapse Prevention," Substance Abuse, Vol. 31, No. 2, April 2010, pp. 108–116.

Witkiewitz, K., G. A. Marlatt, and D. Walker, "Mindfulness-Based Relapse Prevention for Alcohol and Substance Use Disorders," *Journal of Cognitive Psychotherapy*, Vol. 19, No. 3, Fall 2005, pp. 211–228.

Reason Excluded: No MBRP

Witkiewitz, K., S. Bowen, and D. M. Donovan, "Moderating Effects of a Craving Intervention on the Relation Between Negative Mood and Heavy Drinking Following Treatment for Alcohol Dependence," *Journal of Consulting and Clinical Psychology*, Vol. 79, No. 1, 2011, p. 54.

Garland, E. L., S. A. Gaylord, C. A. Boettiger, and M. O. Howard, "Mindfulness Training Modifies Cognitive, Affective, and Physiological Mechanisms Implicated in Alcohol Dependence: Results of a Randomized Controlled Pilot Trial," *Journal of Psychoactive Drugs*, Vol. 42, No. 2, June 2010, pp. 177–192.

Vallejo, Z., and H. Amaro, "Adaptation of Mindfulness-Based Stress Reduction Program for Addiction Relapse Prevention," *The Humanistic Psychologist*, Vol. 37, No. 2, 2009, pp. 192–206.

References

Berkman, N. D, K. N Lohr, M. Ansari, M. McDonagh, E. Balk, E. Whitlock, J. Reston, E. Bass, M. Butler, G. Garlehner, L. Hartling, R. Kane, M. McPheeters, L. Morgan, S. C. Morton, M. Viswanathan, P. Sista, and S. Chang, "Grading the Strength of a Body of Evidence When Assessing Health Care Interventions for the Effective Health Care Program of the Agency for Healthcare Research and Quality: An Update," *Methods Guide for Effectiveness and Comparative Effectiveness Reviews*, Rockville, Md.: Agency for Healthcare Research and Quality, 2014, pp. 314–349. PMID: 24404627

Bowen, S., N. Chawla, S. E. Collins, K. Witkiewitz, S. Hsu, J. Grow, S. Clifasefi, M. Garner, A. Douglass, M. E. Larimer, and A. Marlatt, "Mindfulness-Based Relapse Prevention for Substance Use Disorders: A Pilot Efficacy Trial," *Substance Abuse*, Vol. 30, No. 4, October–December, 2009, pp. 295–305. PMCID: PMC3280682

Bowen, S., N. Chawla, and G. A. Marlatt, *Mindfulness-Based Relapse Prevention for Addictive Behaviors: A Clinician's Guide*, New York: Guilford Press, 2010.

Bowen, S., N. Chawla, and K. Witkiewitz, "Mindfulness-Based Relapse Prevention for Addictive Behaviors," in R. A. Baer, ed., *Mindfulness-Based Treatment Approaches: A Clinician's Guide*, 2nd ed., San Diego, Calif.: Elsevier Academic Press, 2014.

Bowen, S., and M. C. Enkema, "Relationship Between Dispositional Mindfulness and Substance Use: Findings from a Clinical Sample," *Addictive Behaviors*, Vol. 39, No. 3, March 2014, pp. 532–537.

Bowen, S., and A. S. Kurz, "Between-Session Practice and Therapeutic Alliance as Predictors of Mindfulness After Mindfulness-Based Relapse Prevention," *Journal of Clinical Psychology*, Vol. 68, No. 3, 2012, pp. 236–245. PMCID: PMC3902179

Bowen, S., K. Witkiewitz, N. Chawla, and J. Grow, "Integrating Mindfulness Meditation and Cognitive Behavioral Traditions for the Long-Term Treatment of Addictive Behaviors," *Journal of Clinical Outcomes Measurement*, Vol. 18, No. 10, 2011, pp. 473-479.

Bowen, S., K. Witkiewitz, S. L. Clifasefi, G. Grow, N. Chawla, S. H. Hsu, H. A. Carroll, E. Harrop, S. E. Collins, M. K. Lustyk, and M. E. Larimer, "Relative Efficacy of Mindfulness-Based Relapse Prevention, Standard Relapse Prevention, and Treatment as Usual for Substance Use Disorders: A Randomized Clinical Trial," *JAMA Psychiatry*, Vol. 71, No. 5, 2014, pp. 547–556. PMID: 24647726

Brandon, T. H., J. I. Vidrine, and E. B. Litvin, "Relapse and Relapse Prevention," *Annual Review of Clinical Psychology*, Vol. 3, 2007, pp. 257–284. PMID: 17716056

Brewer, J. A., R. Sinha, J. A. Chen, R. N. Michalsen, T. A. Babuscio, C. Nich, A. Grier, K. L. Bergquist, D. L. Reis, M. N. Potenza, K. M. Carroll, and B. J. Rounsaville, "Mindfulness Training and Stress Reactivity in Substance Abuse: Results from a Randomized, Controlled Stage I Pilot Study," *Substance Abuse*, Vol. 30, No. 4, October–December, 2009, pp. 306–317. PMCID: PMC3045038

Carroll, K. M., "Relapse Prevention as a Psychosocial Treatment: A Review of Controlled Clinical Trials," *Experimental and Clinical Psychopharmacology*, Vol. 4, 1996, pp. 46–54.

Carroll, H., *Do Mindfulness and/or Thought Suppression Mediate Treatment Effects on Cardiac Vagal Control in Substance Abusers Treated with Mindfulness-Based Relapse Prevention, Relapse Prevention or Treatment as Usual?* dissertation, Seattle: University of Washington, 2014.

Chan, A. W., J. M. Tetzlaff, P. C. Gøtzsche, D. G. Altman, H. Mann, J. A. Berlin, K. Dickersin, A. Hróbjartsson, K. F. Schulz, W. R. Parulekar, K. Krleža-Jerić, A. Laupacis, and D. Moher, "SPIRIT 2013 Explanation and Elaboration: Guidance for Protocols of Clinical Trials.," *BMJ*, Vol. 346, 2013, p. e7586. PMCID: PMC3541470

Chawla, N., S. Collins, S. Bowen, S. Hsu, J. Grow, A. Douglass, and G. A. Marlatt, "The Mindfulness-Based Relapse Prevention Adherence and competence Scale: Development, Interrater Reliability, and Validity," *Psychotherapy Research*, Vol. 20, No. 4, 2010, pp. 388–397. PMID: 20204916

Chawla, N., "Experiential Avoidance and Substance Use Relapse," dissertation, Seattle: University of Washington, 2011.

Chiesa, A., and A. Serretti, "Are Mindfulness-Based Interventions Effective for Substance Use Disorders? A Systematic Review of the Evidence," *Substance Use and Misuse*, Vol. 49, 2014, pp. 492–512. PMID: 23461667

Collins, S. E., N. Chawla, S. H. Hsu, J. Grow, J. M. Otto, and G. A. Marlatt, "Language-Based Measures of Mindfulness: Initial Validity and Clinical Utility," *Psychology of Addictive Behaviors*, Vol. 23, No. 4, 2009, p. 743. PMID: 20025383

Compton, W. M., Y. F. Thomas, F. S. Stinson, and B. F. Grant, "Prevalence, Correlates, Disability, and Comorbidity of DSM-IV Drug Abuse and Dependence in the United States: Results from the National Epidemiologic Survey on Alcohol and Related Conditions," *Archives of General Psychiatry*, Vol. 64, No. 5, 2007, pp. 566–576. PMID: 17485608

Connors, G. J., S. A. Maisto, and D. M. Donovan, "Conceptualizations of Relapse: A Summary of Psychological and Psychobiological Models," *Addiction*, Vol. 91, No. 12, 1996, pp. S5–S13. PMID: 8997777

Douglas, H. A. C., E. Shilling, and M. K. B. Lustyk, "Stressor Associated Coupling of Heart Rate Changes with Tonic and Phasic Hrv in Polysubstance Abusers Treated with Mindfulness-Based Relapse Prevention, Standard Relapse Prevention, or Standard Aftercare," *Psychophysiology*, Vol. 49, 2012, pp. S38–S39.

Egger, M., G. D. Smith, M. Schneider, and C. Minder, "Bias in Meta-Analysis Detected by a Simple, Graphical Test," *BMJ*, Vol. 315, 1997, pp. 629–634. PMCID: PMC2127453

Florida, D., "Pilot Evaluation of 'Third Wave' Modular Group Psychotherapy for Comorbid Clients," *Australian and New Zealand Journal of Psychiatry*, Vol. 48, 2014, pp. 78–79.

Garland, E. L., *Mindfulness-Oriented Recovery Enhancement for Addiction, Stress, and Pain*, Washington, D.C.: NASW Press, 2013.

Garland, E. L., S. A. Gaylord, C. A. Boettiger, and M. O. Howard, "Mindfulness Training Modifies Cognitive, Affective, and Physiological Mechanisms Implicated in Alcohol Dependence: Results of a Randomized Controlled Pilot Trial," *Journal of Psychoactive Drugs*, Vol. 42, No. 2, June 2010, pp. 177–192. PMCID: PMC2921532

Goyal, M., S. Singh, E. M. Sibinga, N. F. Gould, A. Rowland-Seymour, R. Sharma, Z. Berger, D. Sleicher, D. D. Maron, H. M. Shihab, P. D. Ranasinghe, S. Linn, S. Saha, E. B. Bass, and J. A. Haythornthwaite, "Meditation Programs for Psychological Stress and Well-Being: A Systematic Review and Meta-Analysis," *JAMA Internal Medicine*, Vol. 174, No. 3, 2014, pp. 357–368. PMID: 24395196

Grant, B. F., F. S. Stinson, D. A. Dawson, S. P. Chou, M. C. Dufour, W. Compton, R. P. Pickering, and K. Kaplan, "Prevalence and Co-Occurrence of Substance Use Disorders and Independent Mood and Anxiety Disorders: Results from the National Epidemiologic Survey on Alcohol and Related Conditions," *Archives of General Psychiatry*, Vol. 61, No. 8, 2004, pp. 807–816. PMID: 15289279

Grossman, P., L. Niemann, S. Schmidtc, and H. Walach, "Mindfulness-Based Stress Reduction and Health Benefits: A Meta-Analysis," *Journal of Psychosomatic Research*, Vol. 57, 2004, pp. 35–43. PMID: 15256293

Grow, J. C., *Effects of a Pretreatment Brief Motivational Intervention on Treatment Engagement in CBT-Based and Mindfulness-Based Relapse Prevention*, dissertation, Seattle: University of Washington, 2013.

Grow, J. C., S. E. Collins, E. N. Harrop, and G. A. Marlatt, "Enactment of Home Practice Following Mindfulness-Based Relapse Prevention and Its Association with Substance-Use Outcomes," *Addictive Behaviors*, Vol. 40, 2015, pp. 16–20. PMID: 25218066

Hartung, J., "An Alternative Method for Meta-Analysis," *Biometrical Journal,* Vol. 41, No. 8, 1999, pp. 901–916.

Hartung, J., and G. Knapp, "A Refined Method for the Meta Analysis of Controlled Clinical Trials with Binary Outcome," *Statistics in Medicine*, Vol. 20, No. 24, 2001, pp. 3875–3889. PMID: 11782040

Hasin, D. S., F. S. Stinson, E. Ogburn, and B. F. Grant, "Prevalence, Correlates, Disability, and Comorbidity of DSM-IV Alcohol Abuse and Dependence in the United States: Results from the National Epidemiologic Survey on Alcohol and Related Conditions," *Archives of General Psychiatry*, Vol. 64, No. 7, 2007, pp. 830–842. PMID: 17606817

Hempel, S., S. L. Taylor, N. J. Marshall, I. M. Miake-Lye, J. M. Beroes, R. Shanman, M. R. Solloway, and P. G. Shekelle, *Evidence Map of Mindfulness, VA-ESP Project #05-226*, Los Angeles, Calif.: Department of Veterans Affairs, Veterans Health Administration, Office of Research and Development, and Quality Enhancement Research Initiative, 2014. PMID: 25577939

Higgins, J., D. G. Altman, P. C. Gøtzsche, P. Jüni, D. Moher, A. D. Oxman, J. Savović, L. Weeks, and J. A. Sterne, "The Cochrane Collaboration's Tool for Assessing Risk of Bias in Randomised Trials," *BMJ*, Vol. 343, 2011, p. d5928. PMCID: PMC3196245

Higgins, J. P. T., and S. Green, *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0*, Oxford: Cochrane Collaboration, 2011.

Hsu, S. H., S. E. Collins, and G. A. Marlatt, "Examining Psychometric Properties of Distress Tolerance and Its Moderation of Mindfulness-Based Relapse Prevention Effects on Alcohol and Other Drug Use Outcomes," *Addictive Behaviors*, Vol. 38, No. 3, 2013, pp. 1852–1858. PMID: 23266526

IntHout, J., J. P. Ioannidis, and G. F. Borm, "The Hartung-Knapp-Sidik-Jonkman Method for Random Effects Meta-Analysis Is Straightforward and Considerably Outperforms the Standard DerSimonian-Laird Method," *BMC Medical Research Methodology*, Vol. 14, 2014, p. 25. PMID: 24548571

Irvin, J. E., C. A. Bowers, M. E. Dunn, and M. C. Wang, "Efficacy of Relapse Prevention: A Meta-Analytic Review," *Journal of Consulting and Clinical Psychology*, Vol. 67, No. 4, 1999, pp. 563–570. PMID: 10450627

Katz, D., and B. Toner, "A Systematic Review of Gender Differences in the Effectiveness of Mindfulness-Based Treatments for Substance Use Disorders," *Mindfulness*, Vol. 4, 2013, pp. 318–331.

Kessler, R. C., W. T. Chiu, O. Demler, and E. E. Walters, "Prevalence, Severity, and Comorbidity of 12-month DSM-IV Disorders in the National Comorbidity Survey Replication," *Archives of General Psychiatry*, Vol. 62, No. 6, 2005, pp. 617–627. PMID: 15939839

Lancaster, T., P. Hajek, L. F. Stead, R. West, and M. J. Jarvis, "Prevention of Relapse After Quitting Smoking: A Systematic Review of Trials," *Archives of Internal Medicine*, Vol. 166, No. 8, 2006, pp. 828–835. PMID: 16636207

Lee, K.-H., S. Bowen, and A.-F. Bai, "Psychosocial Outcomes of Mindfulness-Based Relapse Prevention in Incarcerated Substance Abusers in Taiwan: A Preliminary Study," *Journal of Substance Use*, Vol. 16, No. 6, December 2011, pp. 476–483.

Lewin Group and ECRI Institute, *Management of Dyslipidemia: Evidence Synthesis Report. Clinical Practice Guideline*, Washington, D.C.: Veterans Health Administration, U.S. Department of Veterans Affairs, and U.S. Department of Defense, 2014.

Lustyk, M. K. B., H. A. C. Douglas, and E. Shilling, "Tonic and Phasic Cardiac Vagal Control during a Cognitive Challenge in Substance Abusers Treated with Mindfulness-Based Relapse Prevention," *Psychophysiology*, Vol. 49, 2012, pp. S22–S22.

Management of Substance Use Disorders Working Group, *VA/DoD Clinical Practice Guideline for Management of Substance Use Disorders (SUD)*, Washington, D.C.: U.S. Department of Veterans Affairs and U.S. Department of Defense, 2009.

Marlatt, G. A., and J. R. Gordon, *Relapse Prevention: Maintenance Strategies in the Treatment of Addictive Behaviors*, New York: Guilford Press, 1985.

McLellan, A. T., D. C. Lewis, C. P. O'Brien, and H. D. Kleber, "Drug Dependence, a Chronic Mental Illness: Implications for Treatment, Insurance, and Outcomes Evaluation," *JAMA*, Vol. 284, 2000, pp. 1689–1695. PMID: 11015800

Moher, D., C. S. Dulberg, and G. A. Wells, "Statistical Power, Sample Size, and Their Reporting in Randomized Controlled Trials," *JAMA*, Vol. 272, No. 2, 1994, pp. 122–124. PMID: 8015121

Moher, D., S. Hopewell, K. F. Schulz, V. Montori, P. C. Gøtzsche, P. J. Devereaux, D. Elbourne, M. Egger, and D. G. Altman, "CONSORT 2010 Explanation and Elaboration: Updated Guidelines for Reporting Parallel Group Randomised Trials," *BMJ*, Vol. 340, 2010, p. c869. PMID: 20332511

Sánchez-Meca, J., and F. Marín-Martínez, "Confidence Intervals for the Overall Effect Size in Random-Effects Meta-Analysis," *Psychological Methods*, Vol. 13, No. 1, 2008, p. 31. PMID: 18331152

Sidik, K., and J. N. Jonkman, "Robust Variance Estimation for Random Effects Meta-Analysis," *Computational Statistics and Data Analysis*, Vol. 50, No. 12, 2006, pp. 3681–3701.

Skanavi, S., X. Laqueille, and H. J. Aubin, "Interventions Basees sur la Pleine Conscience en Addictologie [Mindfulness Based Interventions for Addictive Disorders: A Review]," *Encephale*, Vol. 37, No. 5, 2011, pp. 379–387.

Substance Abuse and Mental Health Services Administration, *Treatment Episode Data Set (TEDS): 2005—Discharges from Substance Abuse Treatment Services: DASIS Series: S-41*, Publication No. 08-4314, Rockville, Md.: U.S. Deptartment of Health and Human Services, 2008.

———, *Results from the 2010 National Survey on Drug Use and Health: Summary of National Findings*, NSDUH Series H-41, Publication No. 11-4658, Rockville, Md.: Substance Abuse and Mental Health Services Administration, 2011.

Uhlig, Douglas J., "Mindfulness Based Relapse Prevention and the Matrix Model in Substance Abuse Relapse Prevention," *Dissertation Abstracts International—Section B: The Sciences and Engineering*, Vol. 70, No. 4-B, 2009, p. 2596.

U.S. Preventive Services Task Force, *U.S. Preventive Services Task Force Procedure Manual*, Rockville, Md.: Agency for Healthcare Research and Quality, 2008.

Witkiewitz, K., and S. Bowen, "Depression, Craving, and Substance Use Following a Randomized Trial of Mindfulness-Based Relapse Prevention," *Journal of Consulting and Clinical Psychology*, Vol. 78, No. 3, June 2010, pp. 362–374. PMID: 20515211

Witkiewitz, K., B. L. Greenfield, and S. Bowen, "Mindfulness-Based Relapse Prevention with Racial and Ethnic Minority Women," *Addictive Behaviors*, Vol. 38, No. 12, 2013, pp. 2821–2824. PMID: 24018224

Witkiewitz, K., and G. A. Marlatt, "Relapse Prevention for Alcohol and Drug Problems: That Was Zen, This Is Tao," *American Psychologist*, Vol. 59, No. 4, 2004, pp. 224–235. PMID: 15149263

Witkiewitz, K., G. A. Marlatt, and D. Walker, "Mindfulness-Based Relapse Prevention for Alcohol and Substance Use Disorders," *Journal of Cognitive Psychotherapy*, Vol. 19, No. 3, Fall 2005, pp. 211–228.

Witkiewitz, K., K. Warner, B. Sully, A. Barricks, C. Stauffer, B. L. Thompson, and J. B. Luoma, "Randomized Trial Comparing Mindfulness-Based Relapse Prevention with Relapse Prevention for Women Offenders at a Residential Addiction Treatment Center," *Substance Use and Misuse*, Vol. 49, No. 5, April 2014, pp. 536–546. PMID: 24611849

Zgierska, A., D. Rabago, N. Chawla, K. Kushner, R. Koehler, and A. Marlatt, "Mindfulness Meditation for Substance Use Disorders: A Systematic Review," *Substance Abuse*, Vol. 30, No. 4, 2009, pp. 266–294. PMID: 19904664